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Original Communications

THE TREATMENT OF CONGENITAL OPENINGS OF THE RECTUM INTO THE VAGINA—ATRESIA ANI VAGINALIS

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CONGENITAL malformations of the rectum and anus differ widely, but in principle fall into rather definite groups. Trelat made a simple anatomic classification of four groups: (1) strictures; (2) imperforate rectum; (3) absence of the rectum; (4) abnormal fistulous communications. Bodenhammer made a very elaborate clinical classification, naming the numerous types. Atresia ani vaginalis falls into Trelat's anatomic group of abnormal fistulous communications, others of which are the cutaneous openings of the rectum into the perineum, scrotum, sacrum, umbilicus, and the visceral openings of the rectum into the bladder, uterus, and urethra. These abnormal communications of the rectum are predicated on an embryologic failure of closure of the cloaca by the urogenital sinus which normally divides the cloaca into two separate parts, the anterior consisting of bladder, urethra, and vagina, and the posterior which is the rectum. This results in various abnormal openings of the rectum into the vagina, urethra, and more rarely the bladder. In 473 cases of malformations of the rectum and anus collected from the literature by Pennington, 167 were the result of persistence of the original opening of the rectum into the cloaca. There were 67 instances where the rectum opened into the vagina or vulva.

In 162 cases of these malformations occurring in the Boston Children's Hospital during a twenty-five year period, Ladd and Cross report 52 per cent having abnormal fistulous communications, and of these nearly half were rectal openings into the vagina or just outside the hymen.

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Our observations are based on the study and care of six children having the rectal opening inside the vulva just posterior to the hymen which was perfectly formed in all of the cases. In two of the children the vaginal opening of the bowel was small and insufficient so that symptoms of bowel obstruction were in evidence. It is important to think of the possibility of a vaginal opening of the rectum in infants

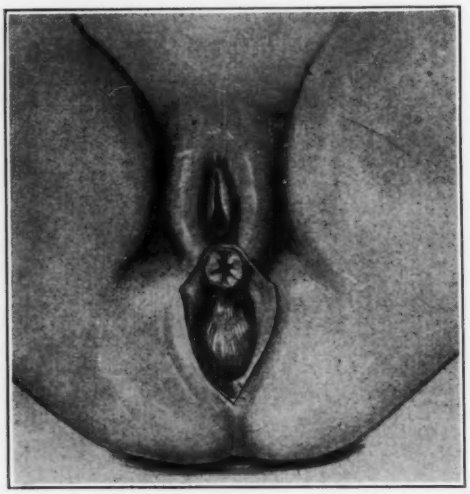

Fig. 1.

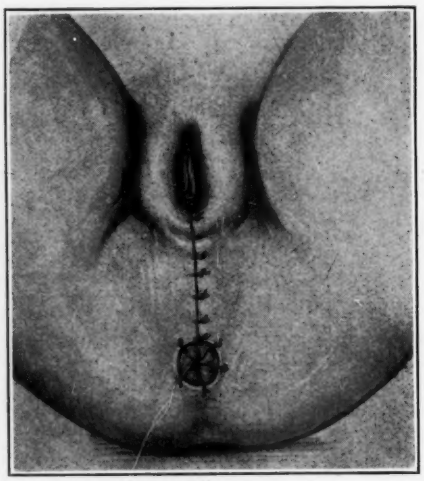

Fig. 2.

Fig. 1.—From second edition Ombredonne, "Chirurgie Infantile." Rizzoli operation —raquet incision exposing the vaginal opening of the bowel as well as the proposed new site for the bowel opening.

Fig. 2.—From second edition Ombredonne, "Chirurgie Infantile." Rizzoli operation completed with bowel opening in normal position and operative defect closed.

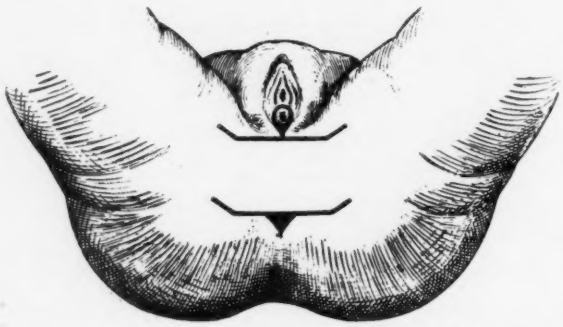

Fig. 3.—From second edition Ombredonne "Chirurgie Infantile." Incisions used for mobilizing vaginal opening of the bowel and for exposing the site of the new anal opening.

born without a normal anus, for the vaginal opening may be small and plugged with dried meconium so that acute obstruction develops. Four of the children had an ample bowel opening in the vagina so that normal movements began early and continued without any evidence of obstruction. In this connection many such patients have lived into adult life without knowing that any deformity existed. Delbet and Brechot quote Le Fort whose patient of forty-eight years of age had

been delivered three times, and neither her doctor, her husband, nor herself were aware of any abnormality until another doctor attempted to make a rectal examination. This strange episode also demonstrates that continence may exist with atresia ani vaginalis. As we have

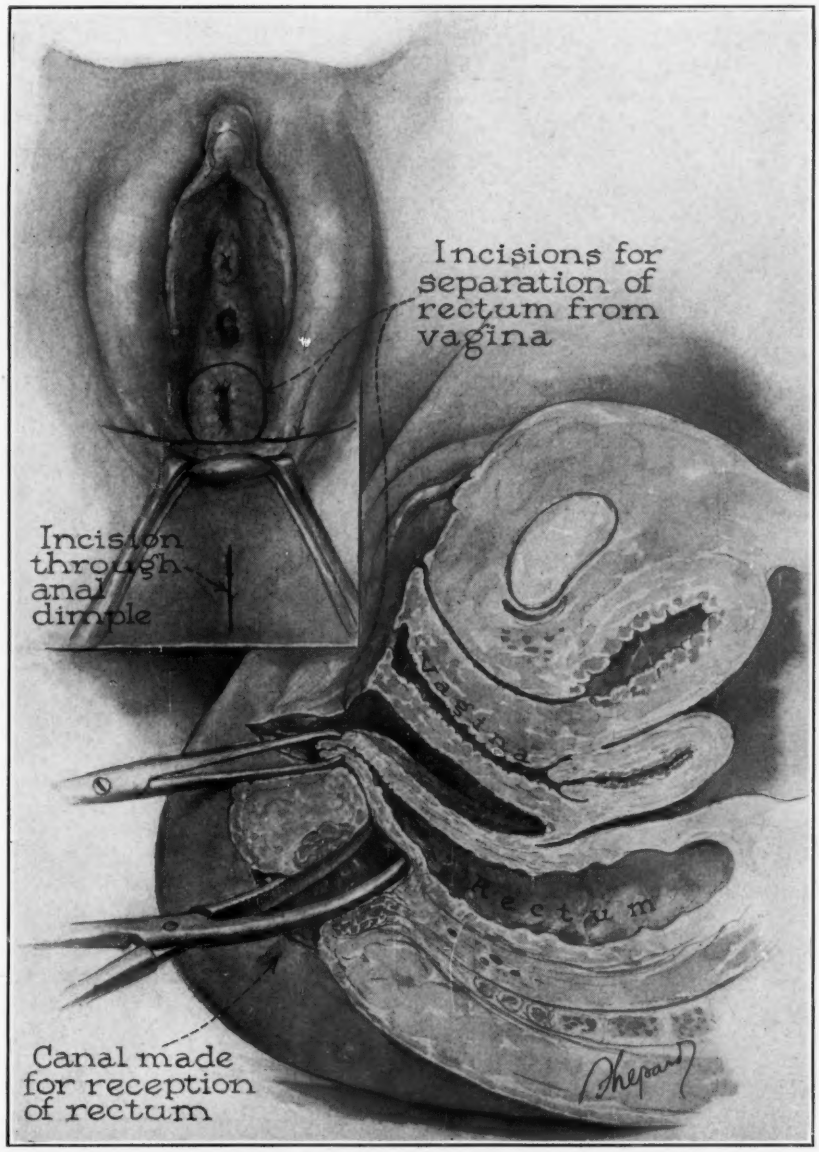

Fig. 4.—Operation carried out. Transverse incision surrounding vaginal opening of the bowel and a small longitudinal incision over the sphincter muscles. Wide mobilization of anterior wall of rectum is necessary.

delayed radical operation in our patients until they were six years of age, we have seen four of these patients develop normal control of the bowel action in its abnormal position, and in two of them there has been a definite separation of the rectal opening from the vagina

so that in one the rectal opening is now perineal and is sufficient and continent. It seems clear that operative interference in these four patients is not indicated, especially in view of the fact that in none

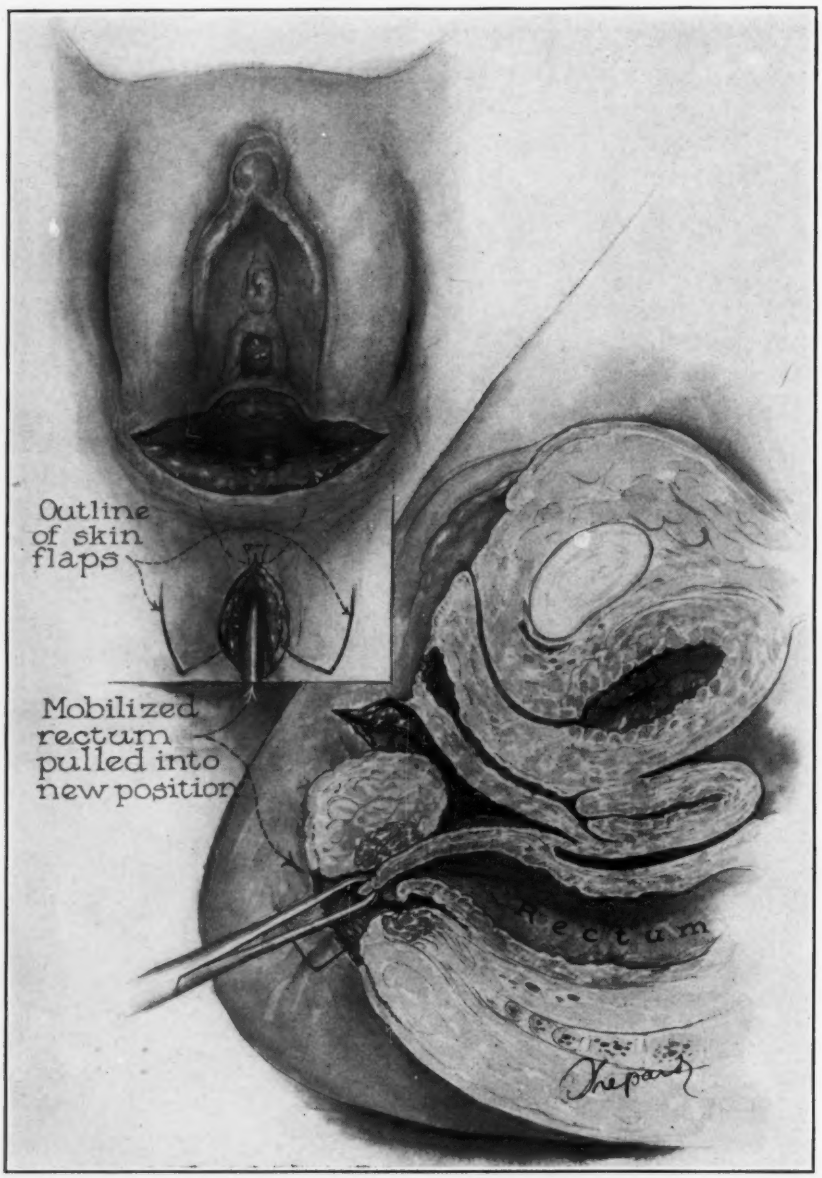

Fig. 5.—Shows formation of skin flaps at new anal opening which are inverted into the space occupied by the anus to be sutured to the terminal bowel.

of the four is there any evidence of the sphincter muscles at the usual anal site. It will be remembered that the sphincter muscles arise around the infolding of epithelium forming the proctodeum or anus. If the anal depression or puckering is absent, the sphincter muscles

are likely also to be absent. This has an important bearing on replacement of a continent vaginal rectum to its normal site where the opening would be largely incontinent.

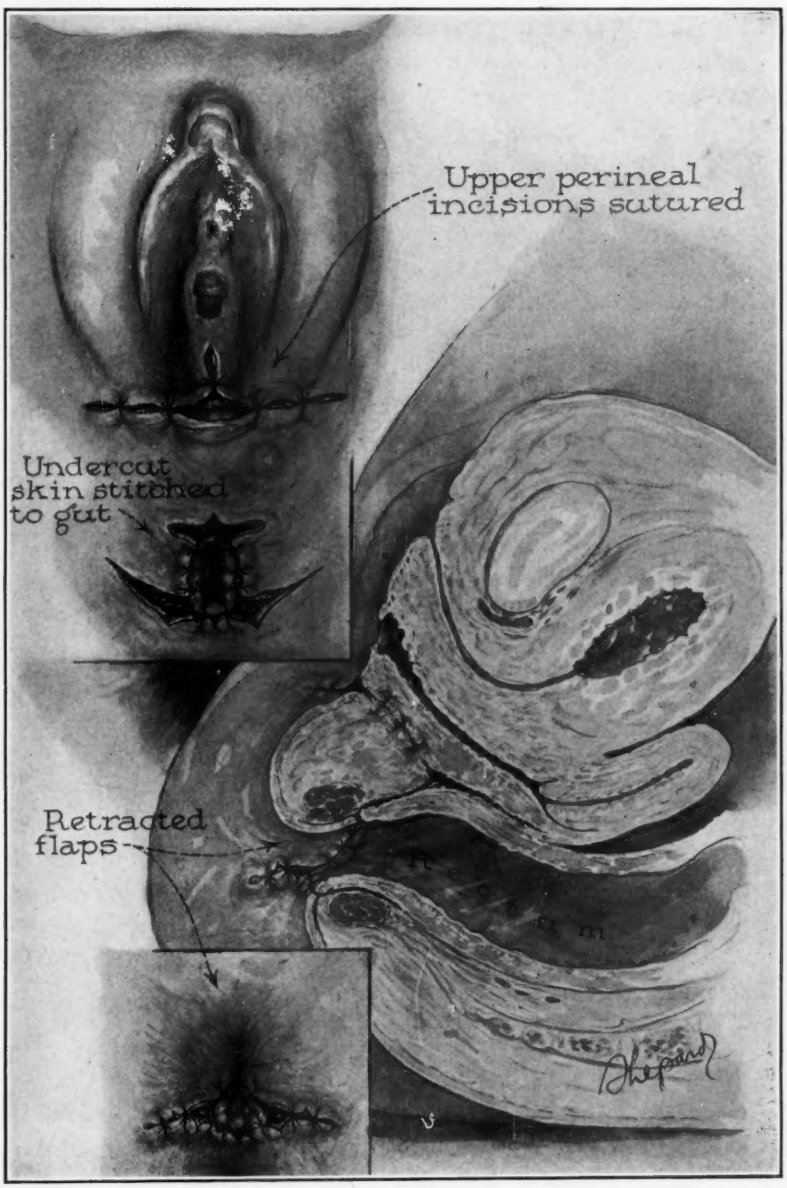

Fig. 6.—Skin flaps inverted into the anal opening and sutured to the end of the bowel. Vaginal defect closed.

Where the vaginal opening is small and insufficient and cannot be dilated and maintained at a proper size, a simple longitudinal division and transverse suture plastic of the rectal opening may be done as a temporary procedure. This was carried out in one infant who later

developed continence and some tendency of separation of the rectum from the vagina. Radical operative replacement of the rectum has not been carried out in this child, who is now seven years of age.

In patients whose vaginal rectal opening is incontinent, radical operative replacement of the rectal opening to its normal site should be attempted. The results are naturally much more satisfactory if the sphincter muscles are present at the site of transplantation.

In a field where no single surgeon's experience has been large, it may be interesting to briefly consider what surgical procedures have been done. Rizzoli, Pierre, Delbet, and Kirmisson have all used a raquet incision surrounding the bowel opening and continuing backward in the midline to the coccyx (Figs. 1 and 2). After separating the bowel from the vagina, the rectum was sewed to the skin in its new position, and the vaginal defect closed. Ombredonne has pointed out the tendency for the newly implanted bowel to retract, so that little by little it tends to assume its original position. Consequently he advocated the useful principle of transverse incisions at the site of the opening of the bowel and its intended site of transplantation (Fig. 3). Harvey Stone has recently reported three successful results using these principles, and we now record two and add what in our hands was a useful step in the operation. Recognizing the great tendency for the anterior wall of the transplanted bowel to retract, and also having had experience with the very annoying mucous discharge when the mucosa of the bowel was sutured to the skin, we have fashioned skin flaps (Figs. 4, 5, and 6), the free ends of which are sutured to the mucosa of the transplanted bowel. When the anterior wall of the bowel retracts, it pulls with it the skin, and thereby lines the anal orifice with skin. If additional skin is necessary to line the anal canal, this may be done at another sitting, forming the base of the flaps posteriorly. Using this principle on both of our operative cases, our patients have not only gained complete control by normal sphincter action, but have an anus lined with skin which affords considerable comfort to them by avoidance of a constant mucous discharge.

FURTHER LABORATORY AND CLINICAL EXPERIENCES IN THE TREATMENT OF CHRONIC, UNDERMINING, BURROWING ULCERS WITH ZINC PEROXIDE

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SINCE the publication of our first reports on the favorable effect of zinc peroxide on anaerobic and microaerophilic infections,[1, 2] we have had an opportunity of studying in some detail nineteen other cases which presented the typical picture of that devastating lesion of the skin and subcutaneous tissues which is caused by a microaerophilic hemolytic streptococcus and is called by the descriptive name "chronic undermining burrowing ulcer." Eight of these cases were seen in other hospitals and were cared for by other surgeons who have been kind enough to let me refer to them in this paper. Such references, however, shall be in general terms only, for these cases may be reported elsewhere by the physicians immediately responsible for them. The present paper is submitted in order to outline in some detail ten new cases of this rare disease (one more is now being treated), which have been cared for at the Presbyterian Hospital, New York City. Some of these cases had certain features which were not associated with the earlier cases, and we have had certain difficulties in the use of the zinc peroxide itself which were not encountered before.

The favorable action of zinc peroxide in the last three cases of the original series[1] was so striking that we fully expected similar results with subsequent patients. There were certain physical properties of the zinc peroxide, however, which seemed to be unfavorable, and we suggested to the manufacturers that an attempt should be made to alter these. The most important of these physical properties were the rapid sedimentation of the material when suspended in distilled water, and the retention of the material in the deep sinuses, owing to its drying or caking propensities. At first we attempted to obviate this by using a suspending medium which would evenly emulsify the material, but it was found that the oils and greases considerably diminished the bactericidal action of the peroxide. Gelatin proved to be a favorable suspending medium, but it had the disadvantage of being a good culture medium for organisms not affected by the zinc peroxide. The manu-

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facturers suggested the use of a 5 per cent pyrophosphate solution properly neutralized with dilute sulphuric acid. This acted as a fairly good suspending medium, but it frequently caused a burning sensation in the wound and occasionally irritated the skin. In order to obviate these difficulties the manufacturers finally decided to change entirely the method of preparing the zinc peroxide. By the new method they obtained a fine white powder which stayed suspended in water, and this seemed to obviate the necessity for using an emulsifying agent.

Just at that time another patient (Case 1) came under our care. The bones of the pelvis were involved in the process and although it was possible gradually to eradicate the disease from the soft parts, the infection spread in the bone, and we ultimately lost the case by the gradual development of amyloid changes in the viscera and the spread of an underlying tuberculosis in the lung. It was noted, however, that although the process in the soft parts improved and eventually healed, the organism did not undergo the characteristic change from hemolytic to green which was seen in the previous cases, and it was felt that at times the zinc peroxide had very little effect; that is, there was a retrogression in healing in the face of what appeared to be an adequate application of the drug. We suspected that the material made by the new process might not be as potent as the original material, but we were assured by the manufacturers that the chemical analysis showed that the new preparation had a somewhat higher percentage of zinc peroxide than the old. We were assured also that the material was very stable and that sterilization did not materially diminish the available oxygen. Our studies in the laboratory, however, seemed to indicate that the new material was not as effective in vitro against the organism as the old material had been, and reports began to come to us, from other surgeons to whom the use of zinc peroxide had been recommended, that different batches of zinc peroxide behaved differently. Some of them seemed to be effective while others seemed to be completely inert. This was particularly demonstrated in the case of chronic undermining ulcer of the axilla of a year's duration which was under the care of W. J. Merle Scott, of Rochester, who will report the case independently in some detail. Suffice it to say, the first material which he received and used resulted in a very striking clinical improvement in the lesion. The lesion responded within a day or two after the application of zinc peroxide, but when a second batch of material was obtained from the manufacturers, the process of healing promptly stopped, the infection began to spread again, and this spread did not stop until another effective material was obtained from the factory and applied.

During this period of uncertainty we had the opportunity of treating two more cases (Cases 2 and 3), the first of which was characterized

by undermining and burrowing rather than ulceration. This occurred in the region of the anus and perineum. It is possible that the toughness of the skin accounted for the nature of the process. The other case presented multiple lesions probably due to autoinoculation. Both areas responded favorably to the close application of zinc peroxide, but one required more extensive operative procedures than the original cases had received; in these cases healing was unaccountably delayed and the favorable change in the organism from hemolytic to green did not take place with the expected rapidity. Furthermore, cases under the care of Carl Burdick, of the Hospital for the Ruptured and Crippled; Fenwick Beekman, at Bellevue Hospital; John Garlock, at Mount Sinai Hospital; Herman Wuerthele, in Pittsburgh, Harry D. Sonnenschein, of the Hospital of Bone and Joint Diseases; James P. Grier, of Evanston, Illinois; and M. J. Henry, of Louisville, Kentucky, behaved in the same way. All of these physicians reported favorable initial improvement following the use of zinc peroxide, with subsequent spread of infection on the continuation of its use. Burdick's patient responded at once to the application of zinc peroxide, but there was one setback lasting several weeks due to an overlooked extension; nevertheless, the wound finally healed in two months. The other patients improved steadily but not with the expected alacrity. Finally, I had an opportunity of visiting those in Evanston and Pittsburgh. It seemed, at the time, as if the zinc peroxide were not being effectively applied to all parts of the wound, and in both instances an operation seemed to be indicated to expose the deep sinuses. These operations were performed and the method of treatment which we had advocated was subsequently carried out by both of the physicians in charge of the cases. Although the patients showed considerable improvement for a short time, they did not do well. Further extension occurred, in one case during continuous treatment with zinc peroxide, and in the other case when the zinc peroxide had been discontinued for a period of three weeks following a skin graft. When activity recurred, both patients decided to come to New York (Cases 6 and 7). About the same time Henry, who had had variable results with zinc peroxide, decided to send his patient to us (Case 5). At the same time a fourth patient was referred independently, who had not been treated at all with zinc peroxide (Case 4). We therefore had an opportunity of studying four cases at the same time, and as we know now, due to the fact that we had a considerable quantity of the old peroxide left, they immediately responded to the treatment. The material which the other surgeons had been using was tested and found to be ineffective.

These experiences of ours, coupled with the experiences of other physicians in various parts of the country, seemed to prove that ineffective preparations of zinc peroxide were being distributed. Some

of these were sent to us to test for potency, and we found almost all of them ineffective. Furthermore, we sent a questionnaire to all of the physicians who had recently received zinc peroxide from the DuPont Chemical Company. Many of these replied that they were not favorably impressed. We finally persuaded the manufacturers that their new method was not producing effective material and urged them to return to the old process. By this time our supply of old material was almost exhausted, and we found it necessary to ask them to make hastily a new batch by the old process. This material was yellow, coarse, and sandy. However, because our supply of the old material was completely exhausted, we had to use the new material on the four patients under treatment. Within two or three days it was evident that the material was not effective. All of the patients showed an increased activity of the infection, with an increase of purulent exudation and a grayish change in the color of the granulation tissue. The new epithelium which had grown in from the margin, as well as the skin grafts which had become fused, began to melt away.

Case 4 showed a deep invasion in the region of the femoral vein which later went on to a suppurative thrombophlebitis, septicemia and metastases, and finally pulmonary embolism and death.

In Case 5, the wound was almost healed and the patient had been promised a discharge from the hospital within a few days, when suddenly a small spot of activity appeared in the middle of the grafted area.

In Case 6, the process, which seemed to have been halted at the ensiform cartilage, burrowed beneath this cartilage over to the opposite side and produced an extensive pocket of pus around the fused cartilages of the sixth, seventh, eighth, and ninth ribs.

In Case 7, the patient suddenly developed erysipelas which spread rapidly from the groin down to the foot, and after treatment with ultraviolet light, which produced a burn, deep abscesses formed in the calf and in the external malleolar region above the ankle joint.

My amazement and discomfiture may well be imagined. We reported the catastrophe to the manufacturers and as soon as possible received from them another batch which was a finely divided white powder similar to the first effective material. They stated that it was the same material only more finely ground. This simple change in the physical state of the material seemed to make all the difference between an ineffective and an effective product. More damage had been done in a few days, however, than could be corrected in as many weeks or months. One patient was lost, one required an extensive operation, one required a number of minor operations, and the fourth patient had to remain in the hospital for two months longer than would have been necessary, if the healing process had continued uninterruptedly, as it almost cer-

tainly would have done if we had been able to continue with the old zinc peroxide. Healing proceeded again slowly but steadily in the three surviving patients. After a short time another batch of the material was sent for trial. We were told that it was prepared in exactly the same manner as the effective material we were then using. We decided to put this to a clinical test by using it on one-half of the wound in Patient No. 6. We soon found that this material did not behave at all like the preceding batch. It hardened and made a plaster-like cast in the wound which moved with each respiration. This caused a superficial erosion of the new epithelium and produced bleeding from the granulation tissue. After three days' treatment it was obvious that this half of the wound was definitely worse, and this retrogression of healing proceeded for a period of about ten days, even after we had returned to the effective material. There seemed to be an inertia of motion which it was difficult to stop. After a period of ten days' reapplication of the effective material, which was continuing its good work in the other two patients, the third patient's wound began to heal again. From that time on, the three remaining cases made steady and uninterrupted progress toward recovery.

The DuPont Chemical Company could not explain why the second batch had this striking characteristic of hardening. We set about, therefore, to study more carefully in the laboratory some of the physical properties of the material. When we suspended the effective and ineffective batches in distilled water, a striking difference in the manner of sedimentation was at once apparent. The effective material sedimented promptly, leaving a clear supernatant fluid, while the ineffective material settled more slowly and left a milky supernatant fluid. In the course of an hour bubbles began to appear in the effective material, while none formed in the ineffective material. After standing for twenty-four hours, the sediment of the effective material became flocculent and curdy and contained numerous gas bubbles, whereas the ineffective material not only remained sedimented but became hard and formed a mould of the bottom of the tube. When these suspensions were set up in tubes which permitted the measurement of the gas, it was found that the effective material produced ten times as much gas as the ineffective in the course of twenty-four hours. An analysis of the gas indicated that at least 95 per cent of it was oxygen. These findings seemed to indicate that the rapid mobility of oxygen might be correlated with the effectiveness of clinical application. But still we could not be sure that the same rapid evolution of gas would take place under the conditions present in the wound. We found that when the zinc peroxide was suspended in broth, the evolution of the gas was markedly decreased, while it was very active in the presence of saline or ascitic fluid or gelatin. The bactericidal action, however, did

take place in broth, even though the evolution of oxygen seemed to be minimal. At this point, although we did not in any sense feel certain that we had found the explanation for the respective activity or inactivity of the various preparations of zinc peroxide, it seemed that we had found a laboratory test which might prognosticate the clinical effectiveness of the material.

At a conference with the DuPont representatives, we asked them to attempt to duplicate the effective preparation. They set about preparing a duplicate product, but the first batch was not successful. The second and the third batches were then prepared, and one of these proved to have the desired qualities, both with regard to laboratory tests and clinical activity.

In the meantime three other cases, having the typical clinical characteristics, and bacteriologic findings of the undermining burrowing ulcer, were referred to us. These were treated with material which we had found to be effective. The infection came under control and the ulcers healed, although there were certain factors in each case which delayed the healing in certain portions of the wound.

During the past year, the DuPont Company has made strenuous efforts to standardize this material. Hal Beans, professor of analytical chemistry, of Columbia University, and Hans Clarke, of the Biochemistry Department of the College of Physicians and Surgeons, have collaborated in this effort, but the physical chemistry has remained obscure. It seems to be a most difficult problem, but the latest reports indicate that its solution has been found, and that effective material will soon be available for all who need it. Our laboratory experiences with zinc peroxide will be reported in more detail at a later date.

OUTLINE OF INDIVIDUAL CASES

CASE 1.—L. L., aged seven years. Unit History No. 417788. Admitted to Babies Hospital June 11, 1934; died Dec. 30, 1934.

History.—Three years before admission this child sustained a fall, injuring her back and right hip. In the region of the right hip there was a large contusion but no radiographic evidence of fracture. Three months later a swelling developed behind the right hip, and an x-ray then indicated the development of a tuberculous process of the right hip joint. She was placed in a cast which, in the course of time, produced an abrasion of the skin of the right sacroiliac region where an ulcer developed, which gradually increased in size. This was thought to be a tuberculous ulcer, but biopsy failed to confirm it. It did not respond to treatment but continued to enlarge. Subcutaneous abscesses developed in the neighborhood, which were opened in various hospitals during the course of a year, but the wounds did not heal. She was finally taken home and for the last year had received very little medical attention. Eventually she was brought to the Babies Hospital in a condition which is most readily understood by a study of the photograph which was taken at that time (Fig. 1). The lesion showed the typical characteristics of a chronic undermining, burrowing ulcer

produced by the microaerophilic hemolytic streptococcus. Over the lower part of the back and sacral region there was a huge ulcer with deeply undermined margins. In the right gluteal region the undermining extended down to the posterior surface of the thigh where the infection had broken out through the skin in many places, forming a "cribriform plate" of the skin of the posterior thigh almost to the knee, with numerous bridges between the openings, some of which were covered with epithelium on the deep, as well as on the superficial, surface. The subcutaneous fat and fascia had been dissolved away, leaving the muscles exposed. Laterally, the undermining extended under the skin into both groins where there were large ulcers just above Poupart's ligament, with subsidiary ulcers nearby and sinuses leading down into the pelvis. X-ray films showed an osteomyelitis of the sacrum, as well as extensive involvement of the ilia and both sacroiliac joints. Cultures revealed a hemolytic streptococcus growing much more profusely anaerobically than aerobically. The ulcerated surfaces were covered with a pale, gelatinous, granulation tissue. In the back new skin had grown down from the upper margin and had extended over a fairly large portion of the ulcerated surface. Since the child was very sick, a

Fig. 1.—(Case 1) Contamination of an abrasion, twenty-five months after onset of disease, showing the extensive undermining of the skin with cribriform openings on back of thigh and over sacrum.

radical procedure was out of the question. She was therefore treated conservatively, and an attempt was made to apply the zinc peroxide to all parts of the affected surface. The powder was suspended in 5 per cent sodium pyrophosphate solution as a thick cream, and the wound was flooded with this material. The wound was then packed with gauze soaked in this suspension and covered with vaseline gauze to prevent evaporation. She began to improve almost at once, but after a period of three weeks of conservative treatment it was obvious that there was not adequate contact with all parts of the wound surface. The undermined skin margins on the back and thigh were therefore excised, leaving a bridge of skin over the lower gluteal region and on each flank. A portion of the skin which was removed at this operation was chopped up into many fine pieces with a tissue chopper and spread over the surface of the wound. These pieces were held in place by a single layer of coarse-meshed gauze which was sealed to the margins with collodion. A considerable number of these "salt and pepper" grafts "took" and were the nuclei of numerous islands of new epithelium.

Following this operation it was possible to get very much better contact of the infected surfaces with the zinc peroxide; granulations took on a healthy red color, and new epithelium grew on the margins as well as from the skin grafts. In the region of the sacroiliac joints, however, the granulations maintained their pale unhealthy appearance, and in these regions the exudation continued to be profuse.

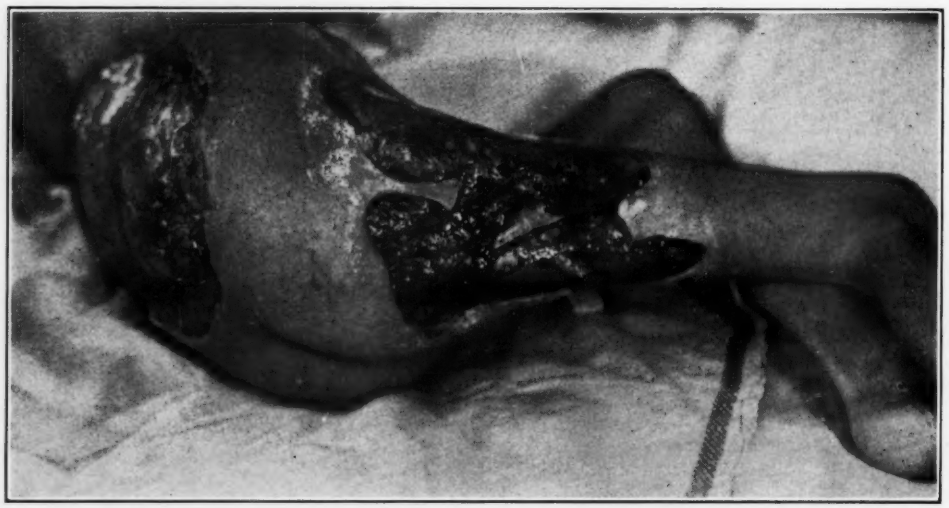

Fig. 2.—(Case 1) After partial excision of the undermined skin flaps; the muscles are exposed, covered only by granulation tissue. The buttock skin was also undermined and had to be incised later.

Fig. 3.—(Case 1) Five months after admission. The skin on the thigh had almost completely healed, but the infection persisted in the sacroiliac joints and the contiguous bones.

Gradually the wounds in the thigh healed, but the infection burrowed down in the region of the anus and resulted in a perforation of the rectum and a contamination of that portion of the field with fecal material. An x-ray study of the pelvis following an injection of zinc peroxide into the sinuses leading down from the groins, showed an extension of the process out through the right sacrosciatic notch into the

tissues of the thigh posterior to the great trochanter. This pocket was opened from without and at the same time an attempt was made to remove as much of the diseased bone as possible on each side of the sacroiliac joints. Although zinc peroxide was immediately applied to the freshly cut bone surfaces, the margin of the excision was evidently not sufficient to permit a control of the infection in the bone, for when granulations developed they had the same pale unhealthy appearance that had been present before.

In the meantime the tuberculous process in the lung continued to advance, and it was evident that we were not going to be able to control either the lesion in the bone or the tuberculous process in the lung. We continued to treat her, however, as best we could, and gradually the wound in the thigh closed as the epithelium grew in from the margins and outward from the grafts. About this time the patient suddenly developed erysipelas, which started from the region of the back and extended all the way down the thigh and leg to the foot. This was controlled with ultra-

Fig. 4.—(Case 2) Contamination of a furuncle or a lymph gland with portal of entry not known. Two years after onset and four days after treatment with zinc peroxide had been begun. (Through a misunderstanding, admission photograph was not taken.) Note the burrowing up into the axilla and the small daughter ulcer above.

violet light and erysipelas serum, but the infection left her in a very debilitated condition. A week later she rapidly lost strength and died, six and one-half months after admission. Unfortunately, postmortem examination was denied by the parents. Figs. 2 and 3 show the progress of wound healing.

CASE 2.—P. D. Unit History No. 438170. Admitted Dec. 8, 1934; discharged April 27, 1935.

History.—A negro, thirty-one years old, was referred from the Southampton Hospital to the Dermatological Clinic and was admitted to the Medical Department of the Presbyterian Hospital under the care of the Dermatological Service, with the following history:

Two years before admission he had developed an abscess in the left axilla which slowly broke down and was opened by his local physician. It failed to heal, con-

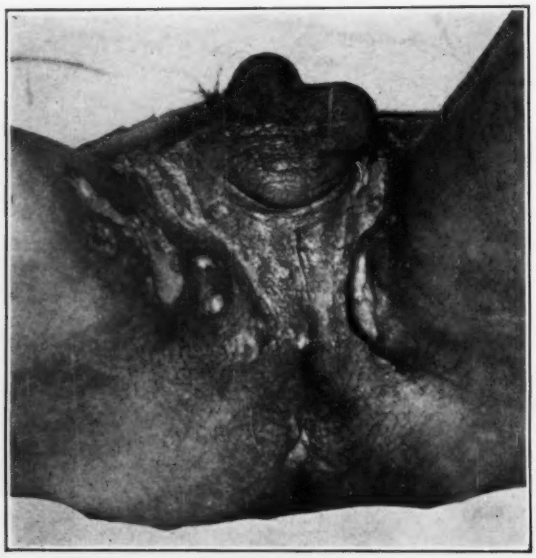

Fig. 5.—(Case 2) Autoinoculation. On admission, one year after onset of lesion and two years after axillary involvement. Extensive burrowing and sinus formation rather than extensive ulceration were the outstanding features of this lesion.

Fig. 6.—(Case 2) Three weeks after zinc peroxide treatment was instituted, axillary burrowing had filled in and new epithelium had covered most of the ulcer.

tinued to discharge, and during the course of six months it was lanced several times. At the end of that time an ulcer began to form, with undermined edges extending down the arm and over the chest wall, and with sinuses leading up into the axilla. This slowly increased in size and a year after the onset a similar lesion began to develop around the anus, which, however, was characterized more by burrowing and sinus infection than by extensive ulceration. But the lesion spread up in the gluteal fold and forward on each side of the scrotum, then upward into each groin, toward the pelvis. Both lesions had steadily increased in extent and had responded to no form of general or local treatment. He was treated on the Dermatological Service for eleven weeks. Biopsies had failed to reveal any tuberculosis, actinomycosis, or other fungi. The Wassermann test was negative; the blood sugar was normal; a

Fig. 7.—(Case 2) Three weeks after excision and zinc peroxide treatment. Wounds are clean and new epithelium has grown in from the margins.

blood count showed anemia and leucocytosis. Aerobic cultures revealed only *Staphylococcus albus*. A specimen of tissue was injected into a guinea pig which was killed six weeks later without any evidence of disease. The Frei test for lymphogranuloma inguinale was twice negative. A series of x-ray treatments caused no improvement. Nonspecific protein was injected without success. Smears showed no amebas. Azochloramide had no effect. He was finally given prolonged baths in potassium permanganate, without any improvement. He was then referred to the Surgical Service where his condition was recognized as that of chronic undermining ulcer due to the microaerophilic hemolytic streptococcus. This organism was found in anaerobic cultures along with several other organisms, namely, hemolytic *Staphylococcus aureus, Staphylococcus albus, Streptococcus viridans,* and *Bacillus proteus.* Because of the

extent of the undermining the patient was treated radically, with excision of the sinus tracts and the overlying skin flaps. The wounds were dressed with a creamy suspension of zinc peroxide in distilled water, after which they were all packed open with fine-meshed gauze saturated with the zinc peroxide suspension and sealed with fine-meshed gauze impregnated with zinc ointment. Improvement was evident within a few days. Pink, firm granulations began to develop from the fresh surfaces and new skin grew in from the margins. In one or two places, however, where the skin tended to roll under, healing was delayed, and from time to time small portions

Fig. 8.—(Case 2) One year after healing, scars soft and pliable, very little limitation of function.

of overhanging or rolled-in skin had to be excised. Nevertheless, the healing process continued favorably and steadily, and the patient left the hospital nine weeks after the beginning of the zinc peroxide treatment (Figs. 4 to 9).

CASE 3.—M. L., aged fifteen years. Unit History No. 444371. Admitted Feb. 11, 1935, and Apr. 29, 1935; discharged Mar. 29, 1935, and May 14, 1935.

History.—Six months before admission this boy had punctured the ulnar border of his right hand with a window screen wire, which lodged there for a few hours before being removed by a local physician who dressed the punctured wound and

bandaged it. It very soon became red, sore, and swollen. After a few days it was opened further and found to be discharging a seropurulent exudate. It failed to heal and six weeks later it was incised again and packed with iodoform gauze. The infection, however, continued to spread, and two months later a third operation was performed. Cultures revealed hemolytic streptococci and other organisms. About a month before admission to the hospital he developed several similar small ulcers on the inner surface of the left thigh and on the outer surface of the left leg near the ankle, which steadily increased in size and did not respond to any form of treatment. On admission, the lesion appeared as shown in Figs. 10, 11 and 12. There was a dirty, irregular ulcer on the ulnar side of the right hand extending posteriorly to the dorsum, with a large area of undermining beneath rolled-in skin margins. This

Fig. 9.—(Case 2) One year after healing, scars soft and pliable, very little limitation of function.

undermining extended also on the palmar surface to a limited degree. The exudate had a very foul odor and cultures yielded not only hemolytic streptococcus, which grew very much more profusely anaerobically than aerobically, but also showed an anaerobic gram-negative bacillus. Cultures from the thigh wound yielded no growth aerobically but hemolytic streptococcus anaerobically. Cultures from the leg ulcer yielded *Staphylococcus albus* aerobically and hemolytic streptococcus anaerobically. It was obvious that we were dealing with a typical case of chronic undermining ulcer due to the microaerophilic streptococcus, and that the lesions on the thigh and leg were of the same nature, probably produced by autoinoculation. We decided to treat the case conservatively with zinc peroxide in the hope of obtaining satisfactory contact with all parts of the infected surface without radical operation. The wound

was therefore flushed with a creamy suspension of zinc peroxide, packed beneath the flaps with fine-meshed gauze soaked in zinc peroxide, and the whole dressing covered with fine-meshed gauze impregnated with zinc oxide ointment. The foul odor of the discharges disappeared at once, and the gram-negative anaerobic bacillus thereafter failed to grow, but the hemolytic streptococcus did not undergo the expected change from hemolytic to green, and after a week of conservative treatment the undermined flaps were excised. This was done satisfactorily, it was thought, on the back of the hand, but we compromised to some degree on the palm in order to avoid extensive loss of tissue (Figs. 13 and 14). The wound was then treated as before with zinc peroxide. Following this treatment granulations appeared somewhat slower than we expected and, much to our disappointment, the hemolytic streptococcus persisted in the culture. When, however, the granulations had grown so as to cover the wound,

Fig. 10.

Fig. 11.

Figs. 10 and 11.—(Case 3) Contamination of small puncture wound. On admission, six months after onset of disease, showing shaggy, gelatinous granulation tissue with undermined and rolled-in skin margins.

we attempted a Thiersch skin graft, but this was completely lost by the collection of pus beneath it. The organism was also found to be particularly resistant to the bactericidal action of zinc peroxide in the test tube, and we came to the conclusion that we were dealing either with an inferior preparation of zinc peroxide or with a particularly resistant organism. Although new skin began to grow in from the margins, it was not uniform, and in three places healing ceased and undermining began again. At the same time the lesions on the thigh and foot which had not been excised showed evidence of activity, with a graying of the granulation tissue and an undermining of the margins, although several of the smaller lesions healed under the zinc peroxide without excision, where apparently contact was more complete. It therefore seemed best to excise the lesion on the thigh and two of the ulcers on the leg. A little later the small areas of undermining at the margin of the hand wound were also

Fig. 12.—(Case 3) Lesions on leg. Autoinoculation. The undermining is not as extensive as in the primary lesion.

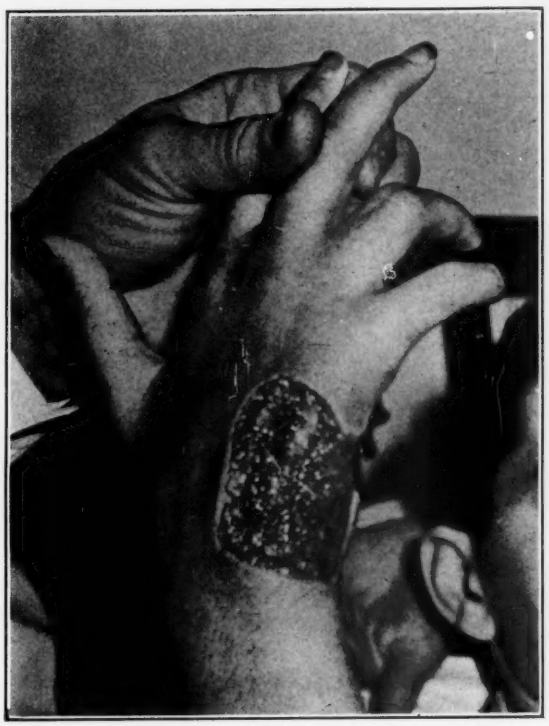

Fig. 13.

Fig. 14.

Figs. 13 and 14.—(Case 3) Undermined skin flaps excised—widely on dorsum, conservatively on palm.

excised, and one by one these came under control; but only after the most careful application of the zinc peroxide by means of small toothpick swabs and close contact of fine silk ribbon soaked in zinc peroxide. The groove on the palmar surface was

Fig. 15.

Fig. 16.

Figs. 15 and 16.—(Case 3) Final healing. Some flexion and adduction contracture but excellent function of the hand.

the last to heal, but finally the cultures became negative and thereafter the wound very promptly closed. The ulcer on the thigh closed satisfactorily after excision,

but one of the leg ulcers was very persistent and required a second excision before it finally yielded to treatment. Figs. 15, 16, and 17 illustrate the final state of healing.

CASE 4.—S. S., aged seventeen years. Unit History No. 454800. Admitted June 3, 1935; died Sept. 7, 1935.

History.—Nine months before admission this girl had scratched her right big toe on a board walk. It promptly became swollen and infected, but the process subsided completely in a few weeks. One month after the toe injury she felt a pain in her right groin, and a swelling appeared. This gradually increased in size and did not respond to local applications of heat, but slowly came to the surface and broke in several places. A physician then connected the sinus openings and it continued to drain. The lesion then spread slowly downward along the inner and anterior aspect of the thigh almost to the knee, and was not checked by repeated operative procedures during the next six months. She had not been confined to bed for any great period of time; but since she ran a moderate fever occasionally, she was confined to the house.

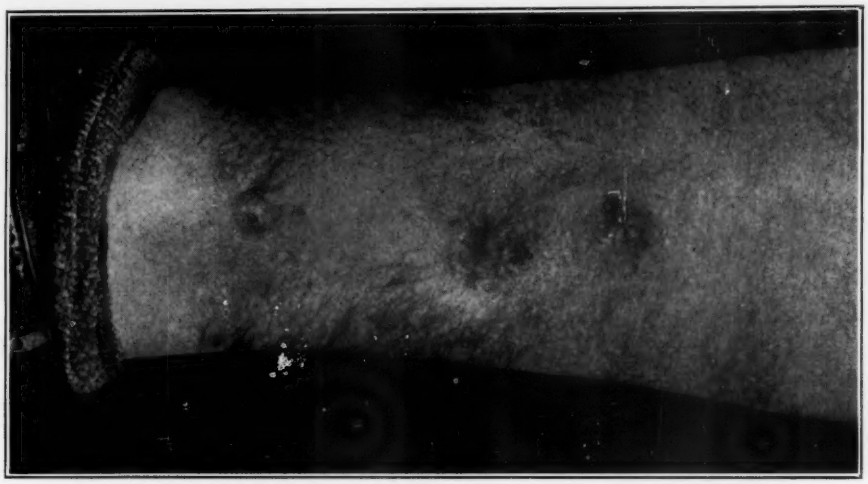

Fig. 17.—(Case 3) Final healing of the leg wound; minimal, flat, soft scars.

On admission to the Presbyterian Hospital the lesion appeared as illustrated in Fig. 18. Below Poupart's ligament there was a large pyriform ulcer with undermined margins extending downward over the anteromedial aspect of the thigh almost to the knee. There were numerous small daughter ulcers which had been produced, not by undermining from beneath but by inoculation from without. Because of her good general condition the lesion was treated conservatively. By that time we were well aware that the zinc peroxide made by the old method was effective and that made by the new method was ineffective. We therefore used only the old material. The wound was dressed with fine-meshed gauze soaked in a creamy suspension of zinc peroxide and sealed with fine-meshed gauze impregnated with zinc oxide ointment. Many of the small daughter ulcers cleared up at once; granulations took on an active red healthy appearance; the undermined margins in many places began to heal, and new skin began to grow in from adherent margins. It was obvious, however, after two weeks of conservative treatment, that there were pockets which were not being adequately reached. These were widely opened, and the lesion was treated radically (Fig. 19). When this operation was done, however, it was seen that the femoral lymph glands around the junction of the saphenous and femoral veins were the site

of deep involvement, so that a compromise was made here. The more superficial glands were removed, but several of the deep glands, which were not more than 3 or 4 mm. in size, were left. Following this procedure, healing progressed very satisfactorily except in the region of the femoral glands, where a swelling occurred in the remaining nodes and a small sinus persisted downward along the nodes to the region of the femoral vein. Also, undermining persisted under the skin of the ab-

Fig. 18.—(Case 4) Lymph gland type. On admission, nine months after onset of illness. Note the gelatinous granulation tissue in the groin ulcer with undermined, rolled-in skin margins. There are numerous daughter ulcers, probably produced by inoculation from without.

dominal wall, making it difficult to get adequate contact in this region. Skin grafts were applied, however, and took well over the lower two-thirds of the lesion, and the process seemed to be in a fair way toward healing (Fig. 20). Just at this stage, our supply of the effective material was exhausted and a new batch, hastily made, which was sandy, coarse, granular, and yellowish in color, was used—not only

on this patient but also on the three subsequent cases of this series, all of which were being treated at the same time. In two or three days it was apparent that the region of the femoral glands and femoral vein was taking on renewed activity. Granulations became pale, the sinus down beneath the glands enlarged, the exudate increased, and the skin beneath the groin became more deeply undermined. Within a week, effective material had been obtained, but the damage had been done. The glands had become greatly swollen, and it seemed necessary to attempt their removal. The patient was therefore subjected to an operation in which the femoral glands were

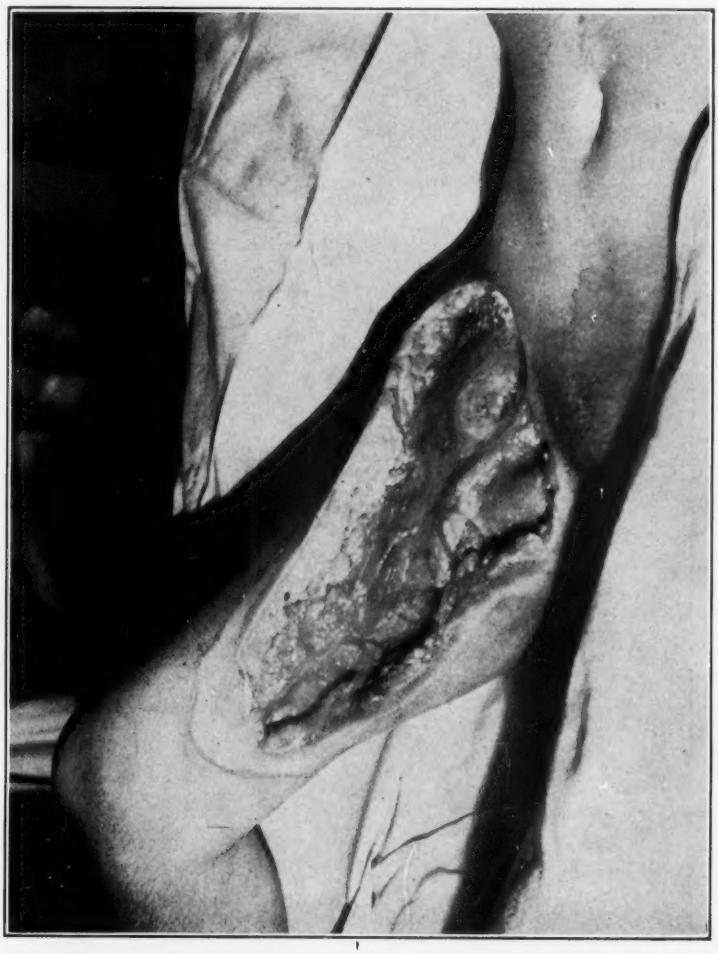

Fig. 19.—(Case 4) After six weeks of conservative treatment, the involved area was finally excised. Extensive burrowing was found, as well as involvement of the glands over the femoral vessels.

removed down to the deep fascia; but in doing so a branch of the femoral vein, possibly the stump of the saphenous which had previously been ligated, was opened, and there was a rush of venous blood from the depths of the wound which could not be controlled except by packing. Following this operation the patient had a high fever and developed a positive blood culture with the hemolytic streptococcus. Pneumonia supervened with an exudation of fluid into the pleura, a culture of which, however, was reported negative. The patient developed a pain in the first left metacarpophalangeal joint which we thought was certain to break down, but which gradu-

ally subsided. She did, however, develop a metastatic abscess in the outer surface of the right leg which had to be incised, and the organism was cultured from it. The temperature gradually came down and the positive blood culture disappeared, but purulent discharge from the depths of the wound steadily increased. A small catheter

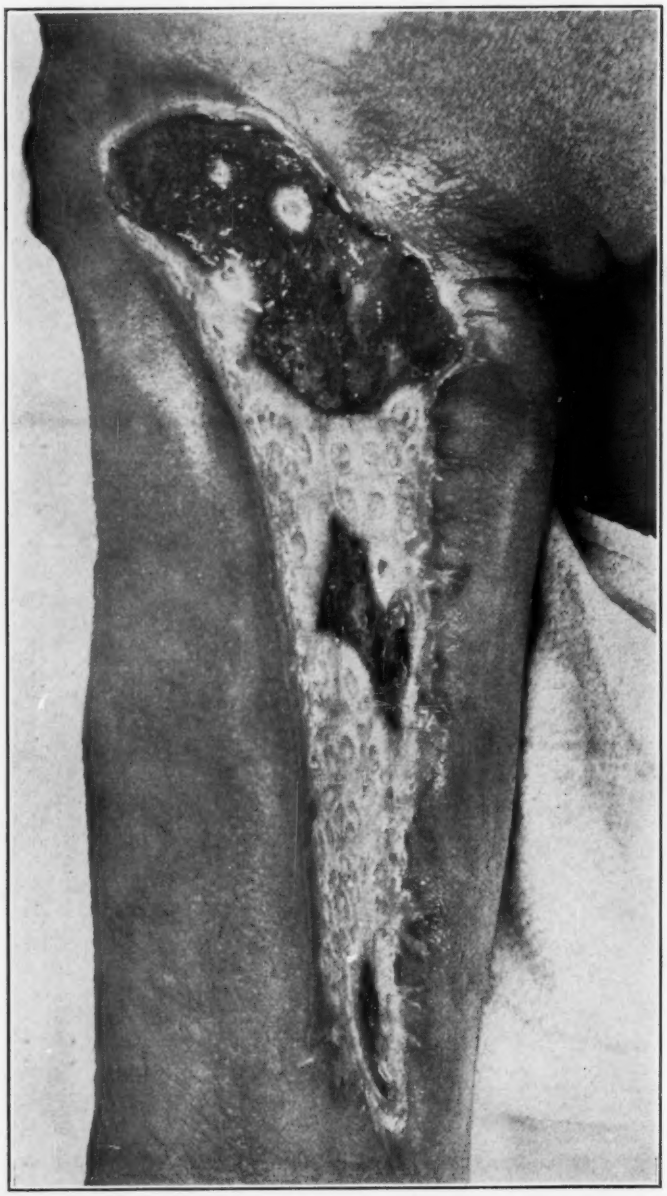

Fig. 20.—(Case 4) Progressive healing of main ulcer. At this stage the supply of effective zinc peroxide became exhausted. Following the application of ineffective material a sinus formed, which extended up into the femoral vein.

passed into the sinus seemed to indicate that it was relatively short, but on the instillation of zinc peroxide the sinus suddenly accepted a fairly large quantity of the material. Very soon the patient said that she felt queer and went into a shaking

chill, with a temporary loss of consciousness. This, however, passed off promptly without a corresponding rise in temperature. Since we believed that a large cavity had been entered, an x-ray film was taken which showed the shadow of the zinc peroxide extending upward along the iliac vessels almost to the midline. It was thought that this represented a sinus tract along the vessels, and after considerable deliberation it was decided that the only hope of recovery lay in the effectual irrigation of this tract. The next day, therefore, zinc peroxide was again injected into the sinus, but this had no sooner been done than the patient promptly became uncon-

Fig. 21.—(Case 4) Autopsy specimen, showing the sinus from the upper part of the ulcer entering directly into the femoral and thence into the iliac vein.

scious and stopped breathing. The heart continued to beat for another ten minutes; but in spite of the very prompt application of the pulmotor, the patient did not respond.

Autopsy showed that this tract, instead of being along the site of the vessels, was actually a suppurative phlebitis of the iliac vein (Fig. 21). The injection of zinc peroxide had blown off the upper end of the thrombus so that both the blood clot and the zinc peroxide embolized into the lung. It is not known, in this case, at just what time the suppurative iliac thrombophlebitis developed, but it is probable that it ap-

peared just before or just after the last operation, and it seems reasonable to believe that this occurred as a result of the application of ineffective zinc peroxide.

CASE 5.—C. S., aged twenty years. Unit History No. 456711. Admitted June 12, 1935; discharged October 21, 1935.

History.—Fourteen months before admission the patient had been operated upon for a recurrent appendicitis. The wound was closed without drainage, became infected, was opened, and continued to drain for several weeks. It then began to show undermining of the skin edges and gradually developed an extensive ulcer which steadily increased in size and spread over the right lower quadrant of the abdomen.

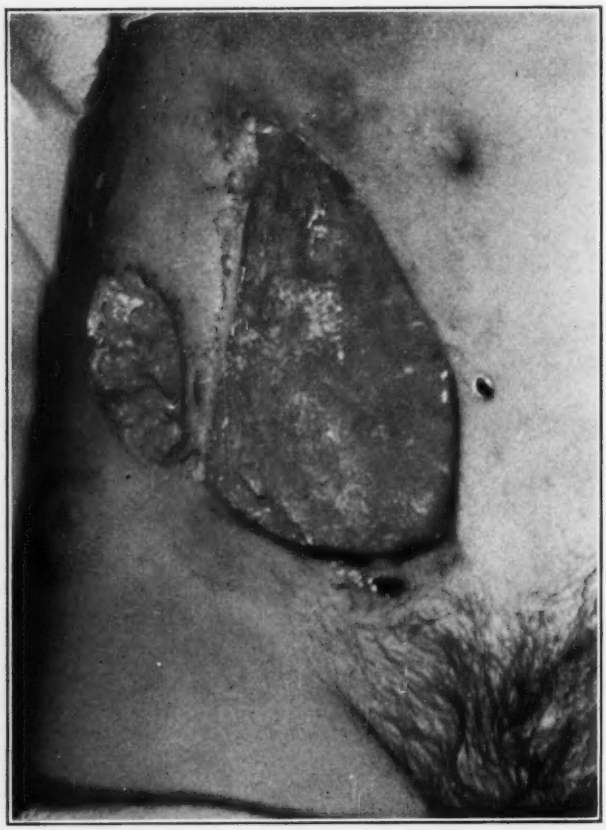

Fig. 22.—(Case 5) Infection of wound following abdominal operation (appendectomy). On admission, fourteen months after onset of illness. Note the gelatinous granulation tissue base, the widely undermined and rolled-in skin margins, the three small and one large daughter ulcers formed by erosion of the skin from beneath, and the bridge of skin.

It was treated with an infinite variety of antiseptics, both mild and drastic, including Harrington's solution, and partial excision was done on occasions; but the process continued in spite of all forms of local and general treatment.

After being ill for eleven months, the patient was sent to the Mayo Clinic where she was treated with local applications of antiseptics without effect. Tissues examined for tuberculosis were negative; blood Wassermann was negative even after the provocative salvarsan. Light treatments were used, cysteine was tried, both without effect. At that time Pemberton wrote to me concerning this

case; he described it and said he thought that it was similar to the ones presented in my previous report. On that basis he had used zinc peroxide, but although his patient showed improvement, the infection did not come under complete control. After two months in the Mayo Clinic, the patient returned home where she continued to receive conservative treatment with zinc peroxide; and

Fig. 23.—(Case 5) Lateral view of the lesion on admission. The skin between the main and lateral ulcers was undermined. Contact of the zinc peroxide without excision was obviously impossible.

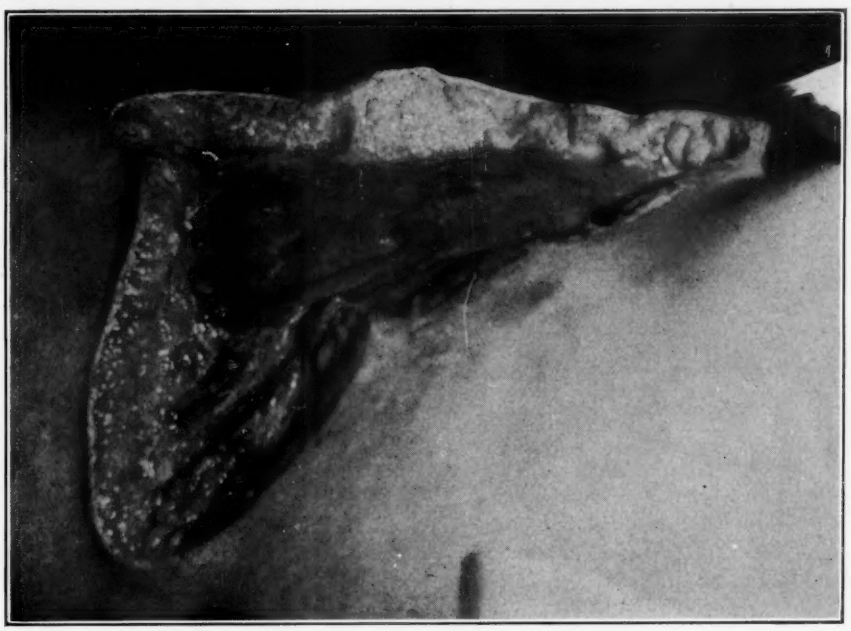

Fig. 24.—(Case 5) Lateral view, six days after admission and five days after excision. Wound appears clean.

although there seemed to be some healing of the ulcer, the infection spread into the flank and up above the umbilicus. She ran a high temperature, varying from 101° to 103° F.; she gradually lost weight, strength, and courage and was finally sent to the Presbyterian Hospital where she arrived in very poor condition. Figs. 22 and 23 show the extent of the wound at that time. There was a large defect in the skin over the right lower quadrant with rolled-in skin edges which were deeply undermined. One small ulcer had formed by perforation from beneath on the inner margin of the wound, another on the lower margin, a large daughter ulcer was present in the region of the anterorsuperior spine, with a bridge of skin, completely surrounded by epithelium, between it and the main ulcer. Above the umbilicus there was extensive undermining with threatened perforation, and in the flank the undermining had spread and broken out as an irregular, roughly circular ulcer, with a considerable amount of adherent subcu-

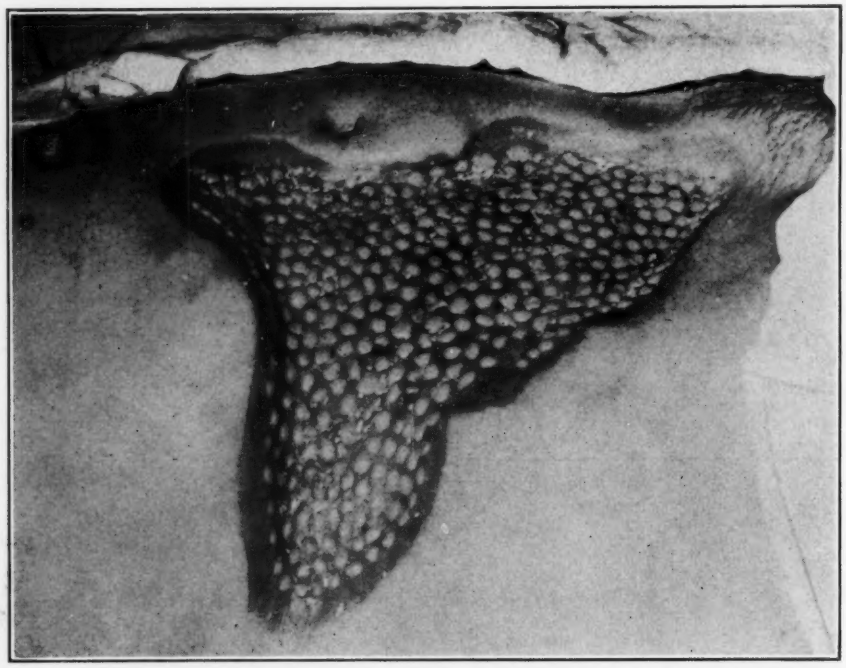

Fig. 25.—(Case 5) Lateral view fourteen days after partial skin graft (on lateral portion) and eight days after the completed skin graft. At this stage the new batch of zinc peroxide was applied, which proved to be ineffective.

taneous slough, but without gangrene of the skin. Since it was apparent that no surface application of zinc peroxide could reach the infection, it was necessary to excise the lesion completely. This was done to the extent illustrated in Fig. 24. All of the indurated tissue was excised, exposing the external oblique muscle. In the region of the umbilicus the margin of excision was narrow, as was also the case in the groin. The wound was immediately flooded with a creamy suspension of zinc peroxide, packed with fine-meshed gauze soaked in the same material, and covered with vaseline gauze. The infection cleared up very rapidly, granulations sprang up actively from all parts of the wound, and new skin began to grow in from the margins. In one spot opposite the umbilicus where the infection had begun to burrow, careful application of zinc peroxide controlled the extension. Sixteen days after the excision a portion of the wound was covered with small pinch grafts which maintained their circulation, and

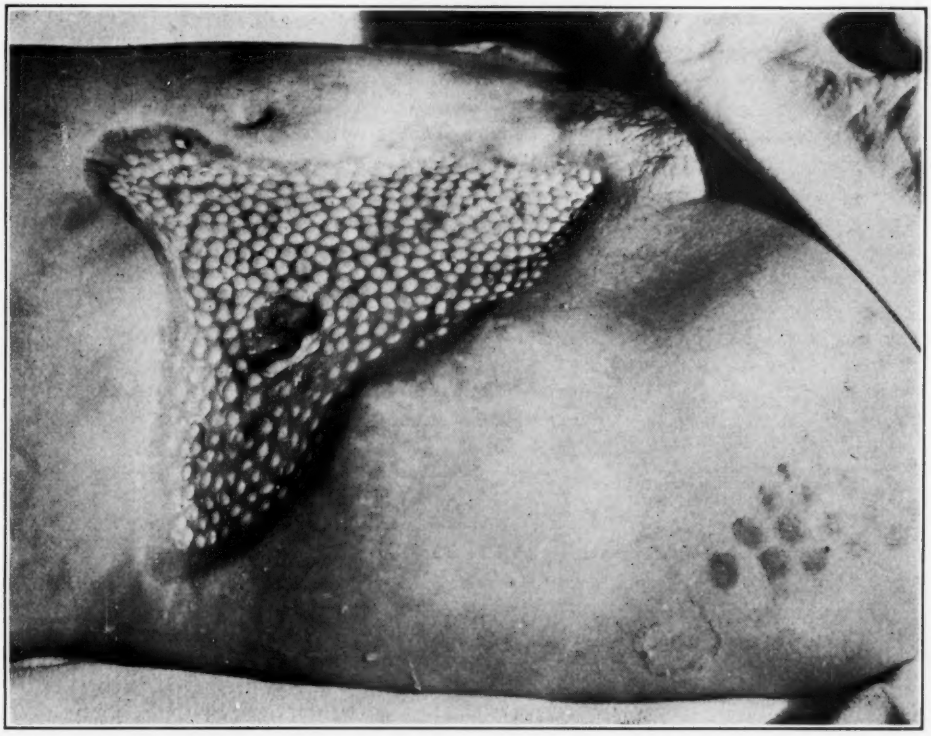

Fig. 26.—(Case 5) Recurrence in center of lesion following the use of ineffective zinc peroxide.

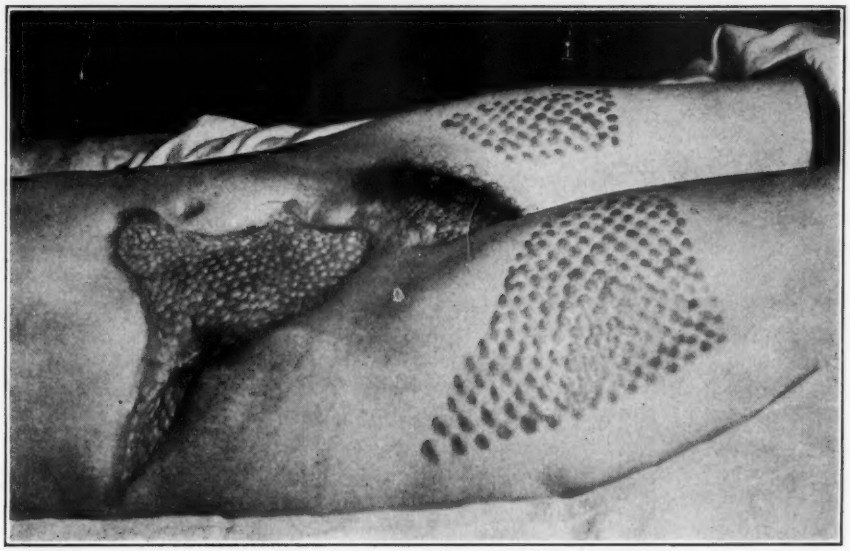

Fig. 27.—(Case 5) Final healing. Note the contraction of the whole area.

six days later the remainder of the wound was covered with grafts (Fig. 25). The healing progressed satisfactorily and preparations were made for the patient to go home. Before this had been accomplished, however, our supply of the old effective zinc peroxide, which we had been using, became exhausted and the hastily prepared material, which was coarse and sandy, was used. Almost immediately a small spot appeared in the center of the grafted area where the organisms burrowed down between the external and internal oblique muscles, and even close application of the zinc peroxide failed to stop the invasion of the organisms which continued even after the application of zinc peroxide which we knew to be effective (Fig. 26). Several local, conservative excisions of this area were required before the infection came under control, but this was finally accomplished. Although the organism recovered from this lesion proved relatively susceptible to the zinc peroxide in the test tube, it was very persistent in this region of recurrence, evidently going down into a fascial space and preventing close contact with the zinc peroxide. Just before closure, however, the hemolytic organism was completely replaced by the aerobic green streptococcus, and soon afterward the wound closed over (Fig. 27).

CASE 6. M. A., aged thirty-seven years. Unit History No. 458354. Admitted July 9, 1935; discharged Nov. 3, 1935.

History.—Nine months previously the patient had been operated upon for what was thought to be chronic cholecystitis. An oblique incision was made in the right upper quadrant and a long, undescended appendix was found to be the cause of his symptoms. This was removed and the abdominal wall was closed without drainage. On the tenth day the wound broke open, revealing a deep infection, and it continued to drain copiously for a number of weeks. Gradually a large ulcer developed, with extensive undermining of the skin margins. The patient ran a temperature of 100° to 104° F. All sorts of local and general measures were used in an attempt to combat the infection, but it continued to spread in spite of everything that was done. He was sent home from the hospital and was treated by his family physician who communicated with me about the case, described the course of events, and stated that he thought that it corresponded to the cases that I had previously described. I advised the use of zinc peroxide, and I was informed that the lesion showed prompt improvement following its application, but while it seemed to improve in certain areas the infection continued to spread in others. Because of this lack of improvement I went to Pittsburgh to see the patient and again concluded that the extent of the lesion and the depth of the undermining prevented adequate contact with the medicine. I advised an excision of the lesion, which had by that time extended upward beneath the costal margin and exposed a portion of the perichondrium of the fused cartilages. The lesion was excised, however, without exposing the cartilages, and the operation seemed to be adequate at the time. This was followed with very careful applications of zinc peroxide, and the patient showed immediate striking improvement; his temperature fell, granulations sprang up all over the surface of the wound, and after sixteen days his surgeon decided to skin-graft. At that time he stopped the use of zinc peroxide. The skin grafts appeared to do well for several days, but after about a week the infection again became active, the skin grafts melted away, the temperature rose, and the skin margins became further undermined. The patient had lost one hundred pounds since the onset of his illness, he was running a high fever, and his prostration was profound. His morale had been completely shattered, and he had lost all expectation of recovery.

The patient was then sent to New York. He arrived in very poor condition; and he had no recollection of the trip. The lesion showed the condition illustrated

in Fig. 28. In the right upper quadrant and right flank there was a large ulcer with grayish surface granulations and rolled-in skin edges with moderate undermining in several places. There was a large area of costal cartilage exposed and an undermining of the subcostal tissues. Likewise, the perichondrial tissues were undermined, exposing an eroded cartilage. It was decided to excise again the overlying flaps and the infected margins. In order to avoid infection of the ribs in the presence of this extensive involvement of tissue, it was decided to cut the cartilage across cleanly near the bone as a temporary measure, with the idea of later removing the cartilage after the infection had been reduced. After excision the wound was flooded with a creamy suspension of zinc peroxide in water, packed with a fine-meshed gauze soaked in the same material, and sealed with vaseline gauze. The wound cleared up rapidly; granulations took on a bright red appearance and sprang up from the recently infected areas, and new skin began to grow in from the margins. Frequent cultures showed a pro-

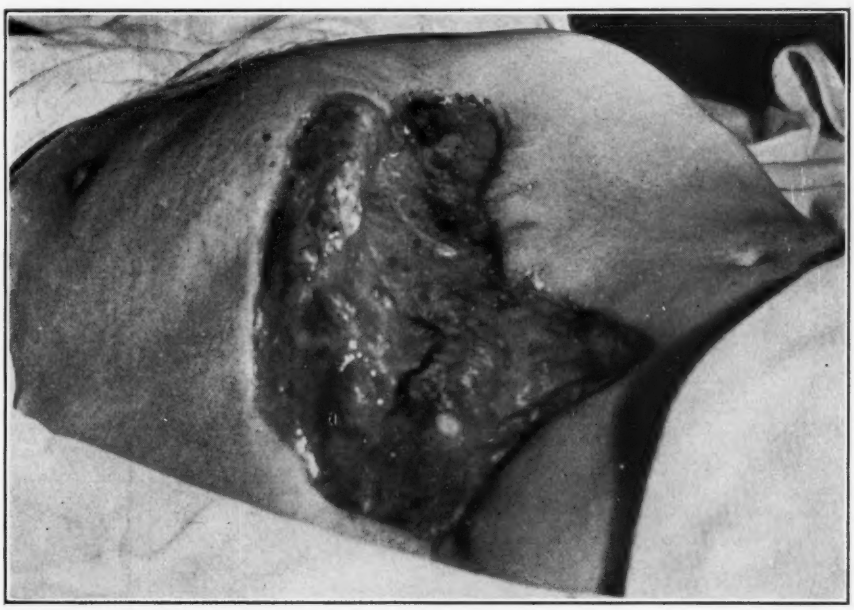

Fig. 28.—(Case 6) Infection of wound following abdominal operation (undescended appendix). On admission, nine months after onset of disease. Note the gelatinous granulation tissue; the rolled-in, undermined skin margins; the exposed cartilage of the twelfth rib; and the exposed perichondrium of the fused ribs.

gressive diminution of the infection, and two weeks after the preceding operation all of the exposed cartilages were removed from the ribs, leaving the bone exposed (Fig. 29). This very promptly granulated without any evidence of invasion of the bone itself. Skin grafts were then applied to the wound in two sittings, and only two or three failed to maintain their nourishment. They soon became fused and began to produce new epithelium. In places, however, the new skin showed a tendency to erode (Fig. 30). This was thought to be due to the mechanical rubbing of the wound by the dressing, resulting from the movements of respiration. Likewise, on two occasions small hematomas formed in the granulation tissue. Just at this time the supply of the old zinc peroxide was exhausted, and the new, hastily prepared, sandy, yellowish material was used. From that time, coincidental with the bad effects produced in the two preceding cases, the wound showed renewed activity of the infection. Pain developed un-

der the left costal margin, and gradually a swelling appeared in that region. It was evident that the infection had undermined the sternum and spread to the other side. Although within a week material known to be effective was applied, the damage had been done, and it was necessary to remove the cartilage of the sixth, seventh, eighth, ninth, and tenth ribs of the left side. When this had been done, the wound responded very nicely; new granulation tissue grew up from the recently cut surfaces and from the bone, and healing progressed steadily (Fig. 31). In the meantime the DuPont Company sent us another batch of zinc peroxide which they said had been made in exactly the same manner as the preceding batch. Although we still had a fair quantity of the effective material, we felt that we should take the opportunity of comparing it with the new product in the same patient. Half of the wound was therefore treated with each prep-

Fig. 29.—(Case 6) Seventeen days after admission. The cartilages of the fifth to the twelfth ribs have been removed, as well as two undermined areas on the opposite skin margin.

aration. We soon found that the two batches had very different physical properties. The new material produced a hard plasterlike cake in the wound, and after three days of its application to the right side, the infection became more active again in that region. The new skin which had formed began to melt away, the margins in several places began to be undermined, and although the effective material was then applied, the retrogression of healing continued for ten days. After the careful application of the effective zinc peroxide, however, the infection again came under control, and from that time the progress of healing was steady. The area on the left was covered with skin grafts which fused gradually and covered over the whole area. Final epithelization, after the organism had disappeared from the wound, was accelerated by the use of oxyquinoline gauze. Fig. 32 shows the final stage of wound healing.

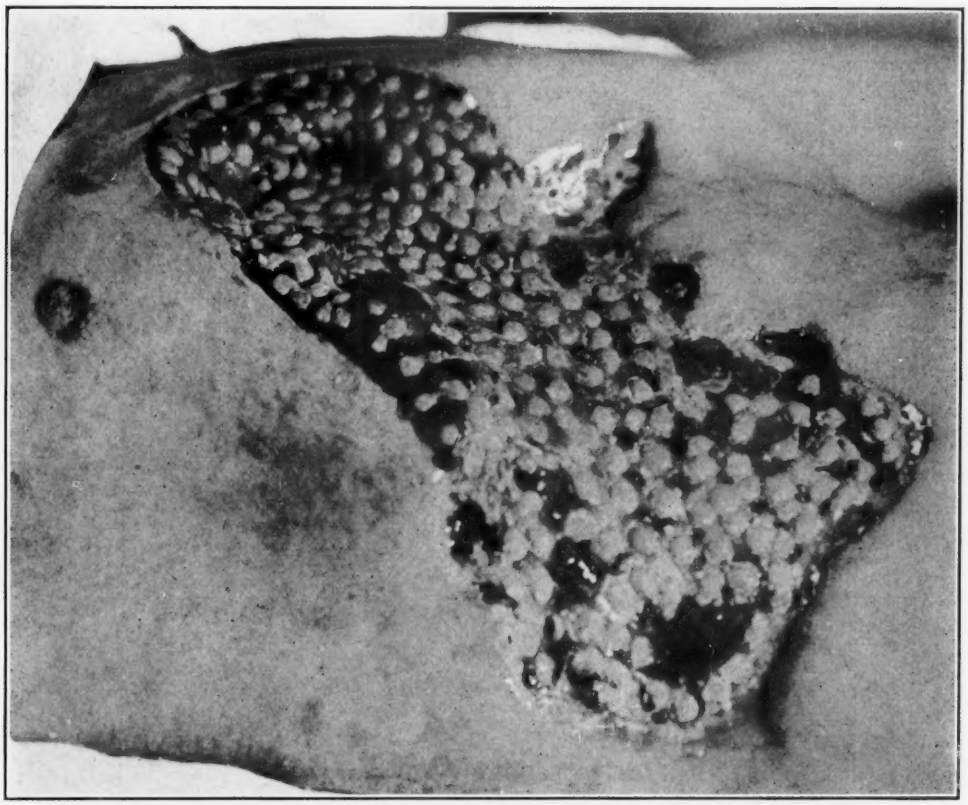

Fig. 30.—(Case 6) Thirty-seven days after admission, twelve days after first skin graft, and five days after second graft.

Fig. 31.—(Case 6) During a period of application of ineffective zinc peroxide the infection spread under the sternum to the opposite side, requiring the removal of the sixth to the tenth costal cartilages on the left. The picture was taken nine days after the operation.

CASE 7.—B. K. B., aged twenty-nine years. Unit History No. 458459. Admitted to hospital July 14, 1935; discharged October 21, 1935.

History.—Fifteen months before admission and one month after a blister had formed on the lower leg from the pressure of a brace, the patient developed a swelling in the right groin which was thought to be a femoral hernia. It did not respond to local applications, and after two or three days it was operated upon. It was found to be a swollen lymph gland which was removed, and the wound was closed. On the second postoperative day the wound became painful, swollen, and tender, and the patient's temperature rose to 103° F., following chills. When the wound was opened, a purulent exudate was found. Infection spread very rapidly in all directions, with a necrosis of the subcutaneous tissues.

Fig. 32.—(Case 6) Final healing of the wound four months after admission.

On succeeding days several attempts were made to halt the spread of the infection by excising the involved skin. The undermining processes, however, continued spreading toward the groin, toward the vulva, and up under the inguinal ligament to the abdomen. Gradually the ulcer enlarged in all directions, the skin edges became excessively undermined, and the margins rolled in. All kinds of local and general treatments, including Dakin's solution, boric acid solution, peptone broth, blood transfusions from vaccinated donors, direct autogenous vaccines, etc., were tried, without effect. The wound was very painful and the temperature ranged from 98° to 101° F. This condition steadily became worse over a period of nine months. Sumner Koch saw the case several times in consultation and suggested that Grier communicate with me. The history of the case seemed definitely to classify it in the group of chronic undermining ulcers and, at my

suggestion, Grier began to use zinc peroxide. Up to that time the patient had been steadily going downhill, and transfusion seemed to be the only means of treatment which was able to halt her rapid loss of strength. Under the zinc peroxide, however, she showed prompt improvement. The surface granulations took on a healthy appearance, but the progress of the infection was not completely checked. Grier found difficulty in applying the zinc peroxide beneath the undermined edges, and he found that the material dried and caked in the wound. The patient made steady improvement for a period of two months, the undermined skin edges filled in, but several deep sinuses persisted, and in these regions the infection continued to spread. Several times the zinc peroxide was given up and other antiseptics were substituted, but invariably the lesion became worse

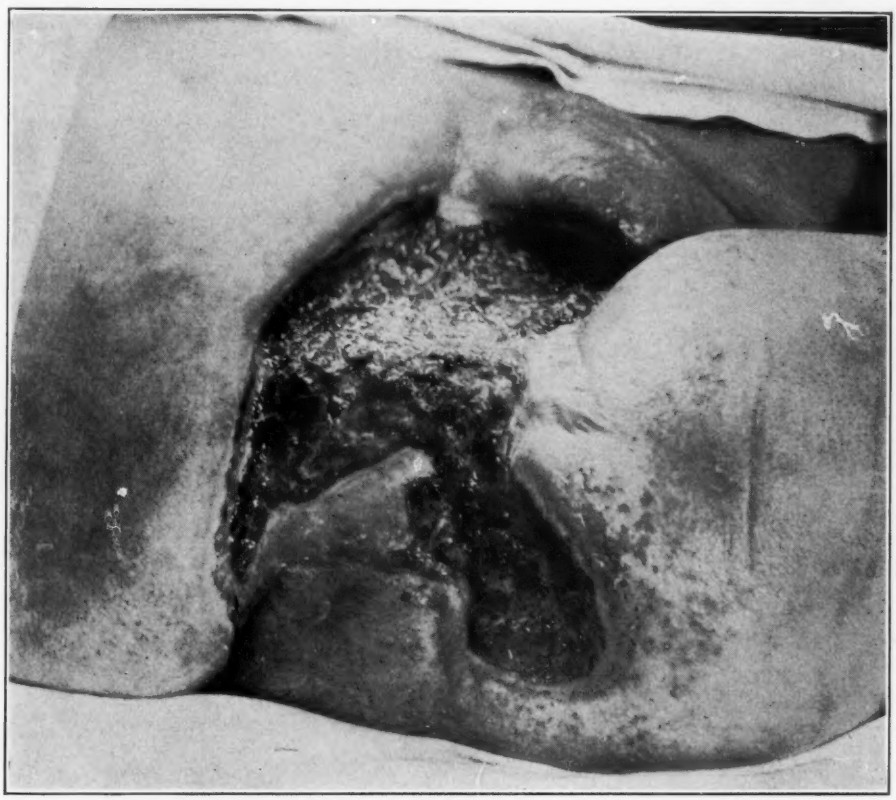

Fig. 33.—(Case 7) Lymph gland type. On admission, fifteen months after the onset of the disease. Note the rolled-in, undermined skin margins.

under such treatment. Finally, a skin graft was attempted, but it was not successful. Grier became convinced that the zinc peroxide was the only medication that would hold the infection in check, but still the wound did not clear up. I offered to go out and see the patient, approximately seventeen months after the onset of the disease. I found that the zinc peroxide was not reaching the depths of the infection and that it had spread across the mons veneris to the opposite side, had undermined the vulva tissues on both sides, and had spread down under the thigh in the region of the anterosuperior spine and the groin. Since it was obvious that a more radical procedure was necessary, the whole lesion was opened widely and all the infected surfaces were left exposed, except for the undermining on the mons veneris. It was decided to make a contralateral incision and

Fig. 34.

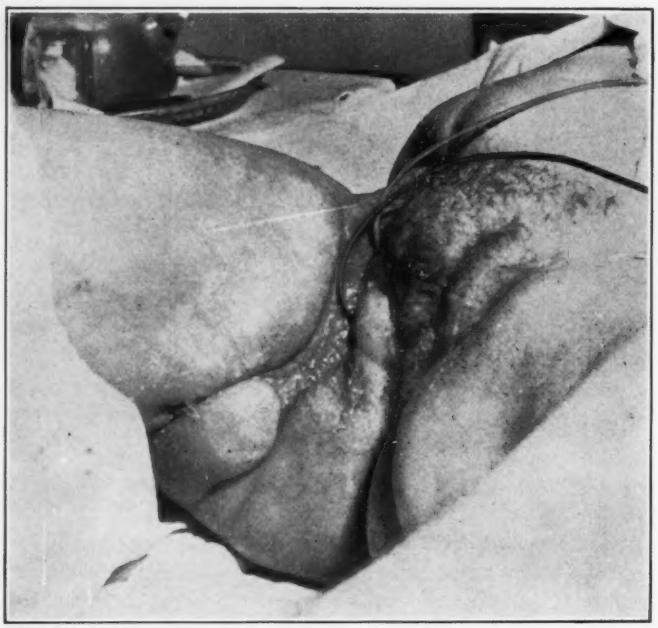

Fig. 35.

Figs. 34 and 35.—(Case 7) Forty-five days after admission; twenty-four days after skin graft. Note the general contraction of the wound. The catheters enter the sinus under the gracilis muscle, which appeared soon after the application of ineffective zinc peroxide, but finally closed when effective material was applied without further excision.

attempt to get contact beneath the skin flap. Following this operation the patient had a very severe reaction, and erysipelas developed, which spread rapidly down the thigh. When she had recovered from the erysipelas, she made rapid progress: granulations grew up from all parts of the wound surface, the wound began to contract, and new epithelium began to grow in from the skin margins. On the inner side of the thigh, however, the infection again spread downward, and Grier sent the patient on to New York where she was admitted to the Presbyterian Hospital.

At that time the wound had the appearance shown in Fig. 33. There was a large granulating area in the right groin which extended up on the abdominal wall and down onto the thigh. In certain portions of the margin there was very extensive undermining, and the skin, which was rolled in, was in contact with the granulation tissue. In other places the skin edges were not undermined, and new skin was growing from these adherent margins. There was a subcuta-

Fig. 36.—(Case 7) Final healing two and a half months after admission.

neous spread, however, on the inner side of the thigh beneath the vulva. These areas were further opened and the rolled-in skin margins were trimmed off. It was then possible to get intimate contact everywhere with a creamy suspension of zinc peroxide in distilled water; the wound was packed with fine-meshed gauze soaked with the same material, and this was sealed over with fine-meshed gauze impregnated with zinc oxide ointment. The granulations promptly became pink, new skin began to grow in from the margins, and on the twenty-first day after admission the whole area was covered with pinch grafts taken from the left thigh. These were held in place by a single layer of coarse-meshed gauze which was sealed to the skin margins with collodion. Then compresses of fine-meshed gauze soaked in saline were applied and sealed with vaseline gauze. The donor area was dressed with zinc peroxide suspension and sealed. After twenty-four hours the saline compresses on the grafted area were removed, the wound was flooded with a dilute suspension of zinc peroxide and again sealed for twenty-four hours, at which time all the grafts had taken on a pink appearance. The

coarse-meshed gauze was then removed and thereafter the wound was dressed in the usual way. Healing progressed steadily thereafter; the grafts promptly fused with each other and with the skin margins, and everything seemed very favorable. Before complete healing had taken place, however, the old effective zinc peroxide, which we had been using, became exhausted and we applied the hurriedly prepared, coarse, sandy mixture, which was used in the three preceding cases. Within a few days there was very evident activity of the infection; the hemolytic streptococcus, which had disappeared, reappeared, and sinuses were apparent where the organism had burrowed during the interval of the application of the noneffective material. One sinus was particularly distressing, as it had burrowed down from the surface and made a communication beneath the gracilis muscle (Figs. 34 and 35). A few days later the patient suddenly developed chills and high fever. Erysipelas appeared at the lower margin of the wound and extended rapidly down the thigh and leg to the toes. In my absence, she was given a treatment with ultraviolet light, to which she had a very severe reaction, developing an extensive burn all over the anterior portion of the thigh and leg, and the posterior surface of the leg. She suffered intense pain and a high fever, and was utterly miserable during this time. The wound became edematous and some of the new epithelium dissolved. It gradually subsided on the thigh, although deep sinuses formed in the calf and in the lateral surface of the ankle above the malleolus and on the dorsum of the foot, which required incision. These lesions were treated with zinc peroxide and gradually cleared up. The wound healing continued, the sinuses closed, and finally the whole area became covered with epithelium (Fig. 36).

CASE 8.—C. B., aged thirty-nine years. Unit History No. 475112. Admitted to Presbyterian Hospital Dec. 23, 1935; discharged March 4, 1936.

History.—A year and a half before admission the patient received a small abrasion on the right forearm, and a few days later developed a gland in the axilla. This gradually softened and was opened by his local physician. Pus was released but another gland developed, below the first one, on the chest wall, beneath the margin of the pectoral muscle. Several days later this was also opened and both wounds continued to discharge purulent material, showing no tendency to heal. Finally the infection began to undermine the skin. The lesion spread forward beneath the right breast, upward into the axilla, beneath as well as superficial to the pectoral muscle, and likewise downward and backward on the chest wall. The edges became extensively undermined, and infection broke through the deep surface of the skin, forming daughter ulcers below and to the inner side of the right breast and up in front of the right shoulder. He was treated with all sorts of antiseptics, but nothing seemed to check the infection. He was then sent to New York where John Joseph Eller, a dermatologist, made a diagnosis of syphilis. Although there had been no history of syphilis, the Wassermann was 2+. Very intensive antisyphilitic treatment caused no improvement in the lesion, and the Wassermann remained unchanged.

Eller then referred the patient to me, and he was admitted to the Presbyterian Hospital when the condition had reached the stage shown in Fig. 37. On the chest wall near the axilla there was a large irregular oval ulcer, measuring approximately 6 by 15 cm., with the long diameter transverse. This was bridged by a strip of skin which ran transversely, dividing it into two parts. Below the main ulcer there were three small daughter ulcers which had evidently formed from invasion of the organism from the surface. There was extreme undermining posteriorly, extending backward about 6 to 8 cm. There was also undermining up into the axilla and under the pectoral muscle. At the inner side of the nipple

there was another ulcer with undermined edges which was connected with the main ulcer by a sinus beneath the nipple. The margins of this daughter ulcer were considerably undermined on the inner and upper sides. In the infraclavicular region there was another daughter ulcer, evidently produced by autoinoculation. This had deep undermined margins but was partially covered by a thin, tenuous, weblike veil of thinned-out skin, perforated in several places, leaving bridges between the openings; and epithelium grew on the deep as well as on the superficial surface. On the anterior part of the shoulder, over the pectoral muscle, there was another smaller oval ulcer with undermined margins. In several places the skin was rolled under, and in the center of the main ulcer there was a deep area of greenish gray granulation tissue extending down between two of the ribs. The first procedure was to cut off the bridge of skin across the ulcer, which permitted a better application of the medication to the undermined flaps. We decided to avoid a radical procedure at first because we

Fig. 37.—(Case 8) Lymph gland type. On admission, eighteen months after the onset of the disease. Note the bridge of skin and the daughter ulcerations, some formed from within and others from without. There is extensive undermining up over the pectoral muscle and posteriorly, moderate undermining everywhere else.

were anxious to conserve as much as possible of the skin of the axilla. The zinc peroxide, therefore, was applied in a creamy suspension, the wound was packed with fine-meshed gauze soaked with the same material, and this was sealed over with fine-meshed gauze impregnated with zinc oxide ointment. Granulations at once began to take on a pink healthy appearance; the undermined flaps began to seal down and new skin began to grow in from the margins (Figs. 37 and 38). The weblike skin over the daughter ulcers on the inner side of the breast and in the infraclavicular region was trimmed off because the epithelium had grown on the deep surface, and the skin margins were rolled under. When this had been done these ulcers promptly closed. At the end of the fourth week the rolled-in skin was also trimmed back from the margin of the main ulcer, and the deep portion of the infection which went down between the ribs was completely excised. The undermining in the axilla steadily filled in without any radical operation in this area. Under the breast a small sinus, through which

the medial daughter ulcer communicated with the main ulcer, persisted, but this was not opened because we felt we were getting good contact and hoped that it might close following irrigation with zinc peroxide. On the tenth day after excision of the margins, the area was covered with skin grafts of the Reverdin type. These were held in place with a single layer of coarse-meshed gauze sealed to the neighboring skin with collodion, but because of the concavity of the axilla and the movement of the arm, it was not possible to maintain contact with all of the grafts, and about six out of thirty were lost. The others, however,

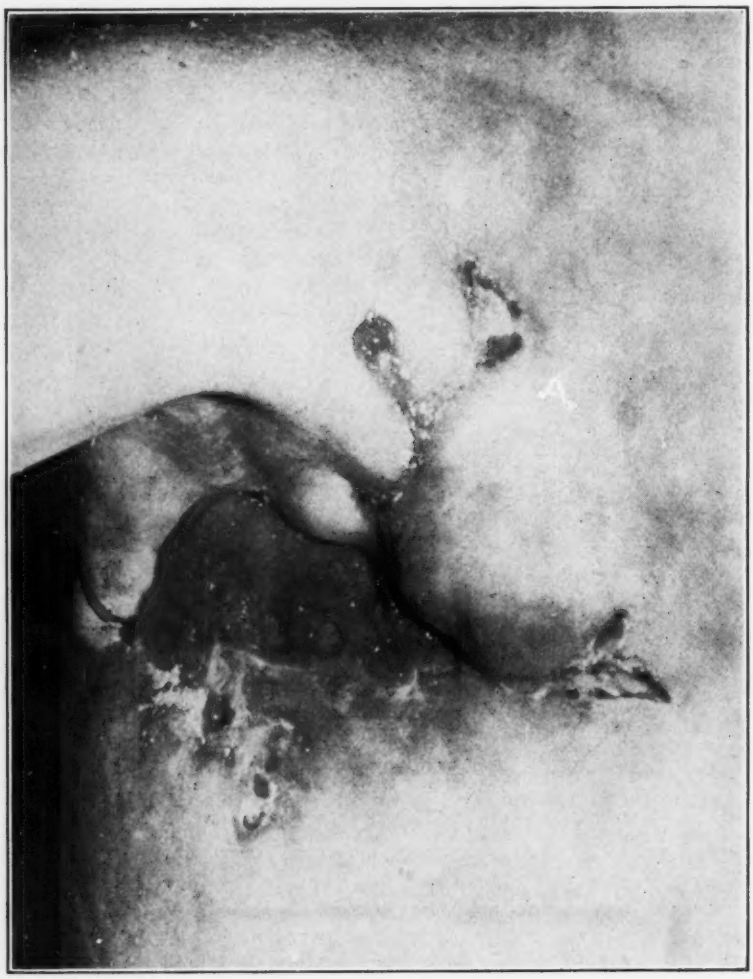

Fig. 38.—(Case 8) Twenty-five days after admission. The wound has cleared up considerably without extensive excision, but sinuses persist under the breast and down between the ribs. Undermining persists posteriorly and up toward the pectoral muscle.

soon fused with each other and with the neighboring skin. The sinuses into the axilla and beneath the pectoral muscle gradually closed, but the inframammary sinus persisted (Fig. 39). It was then decided to hasten the closure of this sinus by opening it widely. There were evidently nooks and crannies which were not getting proper contact. When this sinus was opened, the granulations soon took on a pink appearance, the wound began to contract, and new skin grew in from the margins. During the course of treatment the hemolytic organisms very

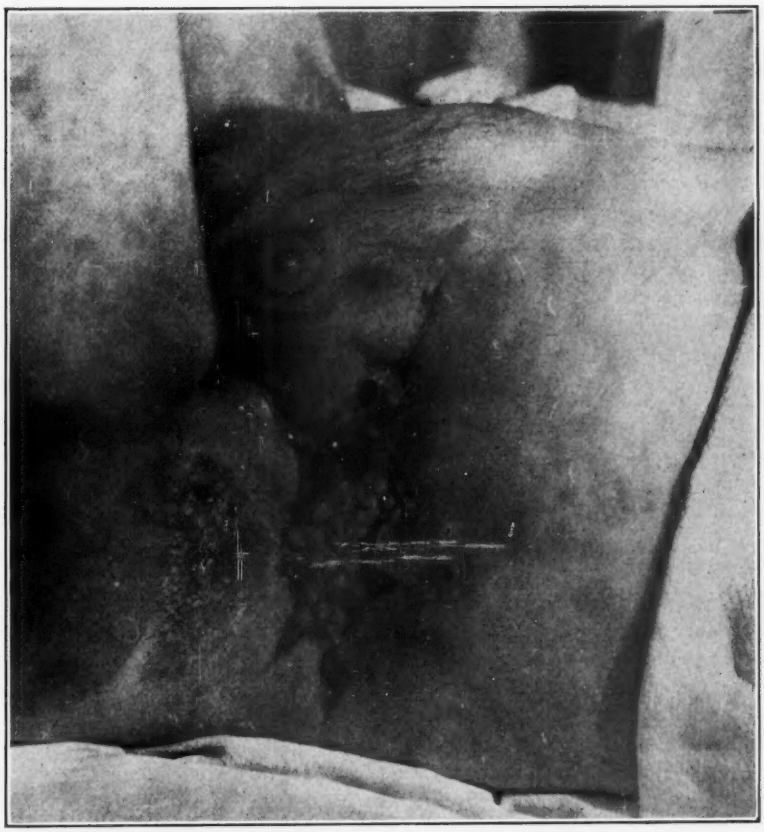

Fig. 39.—(Case 8) Two months after admission; three weeks after skin graft. The sinus under the breast and the small one down between the ribs persisted and had to be excised.

Fig. 40.—(Case 8) Final healing with perfect function of arm.

promptly disappeared from those portions of the wound which were getting the best contact with the medication, and were replaced by green aerobic streptococci. For a considerable time, however, the hemolytic organism persisted in the sinus under the breast and in the central depression between the ribs. When these were opened widely, application was more effective, and healing finally took place. One of the small daughter ulcers on the chest wall, which we thought had formed by inoculation from without and which showed no deep connection with the main ulcer, persisted after all the rest of the wound had healed, and the cultures remained positive until it was completely excised. Within three days after this excision the culture became negative, and the wound rapidly closed (Fig. 40).

CASE 9.—G. R., aged eighteen years. Unit History No. 467841. Admitted to Presbyterian Hospital October 20, 1935; discharged August 4, 1936.

History.—Sixteen months before admission this boy fell from a bicycle and abraded the outer side of his left knee. Although it was superficial, the wound became infected. In spite of the application of various antiseptics while under the care of several doctors, the wound showed no sign of healing for a period of two months. Then three small lesions appeared in the neighborhood of the central ulcer. Ultraviolet light was then applied, and there seemed to be an effort toward wound healing. The small lesions persisted, however, and some weeks after that a physician probed them and found extensive undermining. Merthiolate, mercurochrome, Dakin's solution, bacteriophage, and balsam of Peru were applied again and again, without effect. At times there seemed to be some healing, but the lesion slowly and relentlessly spread. One day the wound was accidentally hit with a tennis racket, and the infection immediately took on renewed activity. Another surgeon was called in who decided to incise the lesion. After removing some of the deeply infected tissues, he sutured the skin together. This very promptly broke down, and the lesion took on a much more active spread; the leg began to swell, and the glands of the groin became enlarged. The infection spread across to the inner side of the knee. The patient was taken into the University Hospital in Chicago, where further incisions were made. Boric acid and Dakin's solution were used locally and ultraviolet light as well. The leg became steadily worse, the tissues sloughed away, and the ulceration spread upward over the anterior surface of the thigh. He was then treated by a succession of doctors, each of them trying something new. Potassium permanganate was used for three weeks, without result. Serum and tin were tried for six weeks more, without result. The original family physician then took over the case again and applied silver nitrate, Dakin's solution, antiphlogistine, ichthyol, mercurochrome ointment, boric acid, and potassium permanganate, in order, all without avail.

During the treatment the ulcer steadily progressed and daughter ulcers formed by perforation of the skin from beneath, but in places the wound showed evidence of healing. A culture from the wound was reported negative. The patient was then sent to Phemister, who advised the discontinuance of all local treatment, sent him to Florida, and advised him to leave the wound exposed to the sunshine. The patient carried out this treatment, but the infection steadily progressed, and he was finally taken to the hospital where local treatment with various antiseptics was again used. Several new ulcers formed during this time and a number of relatively limited operations were performed in an effort to open up some of the undermined pockets. Dakin's solution, potassium permanganate, silver nitrate, magnesium sulphate, and boric acid were all tried.

At that stage Duncan Owens of Miami Beach, who was in charge of the case, communicated with me. He reviewed the history and described the lesion. Be-

lieving that the case belonged to this group, I advised the use of zinc peroxide The lesion very promptly showed a favorable reaction to the treatment. Active granulations appeared and new skin began to grow in from the adherent margins The infection, however, continued to spread in certain directions, and the patient finally returned to Chicago and put himself under Sumner Koch's care. Again, various antiseptics were applied; zinc peroxide was used on several occasions, but not consistently, and the infection spread, particularly on the outer side of the thigh, burrowing down between the biceps muscle and the bone. In spite of

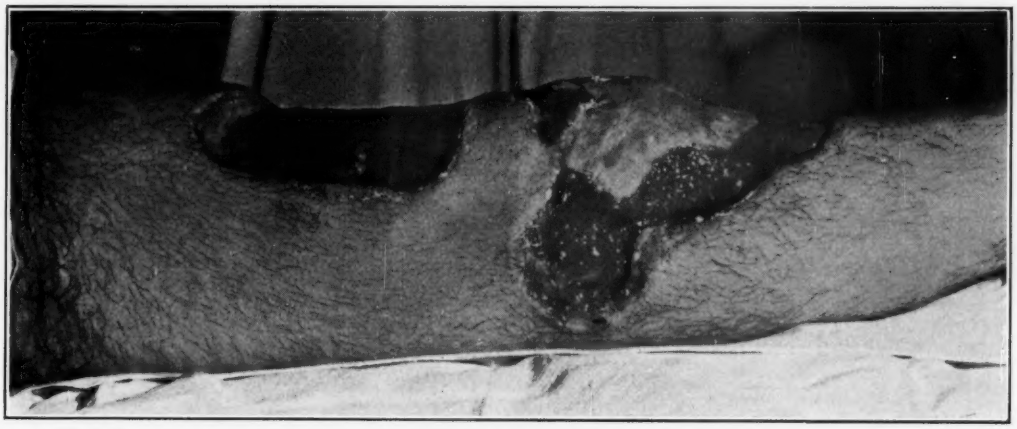

Fig. 41.—(Case 9) Contamination of an abrasion. On admission, sixteen months after the onset of the disease. Medial view. Note the absence of new epithelium at the skin margins, which are moderately undermined in several places.

Fig. 42.—(Case 9) On admission. Lateral view. Note the deep groove beneath the biceps muscle and the sinus into the infrapatellar bursa, as well as the undermining into the popliteal space and the upper posterior thigh. There are two islands of new epithelium around the patella.

every treatment the infection continued to advance. At one time the patient was given continuous soaks in the tub, but nothing seemed to halt the progress of the infection. Finally, after five months, Koch sent him to New York. At this time, sixteen months after the the onset of the infection, the lesion appeared as is shown in Figs. 41 and 42.

There was a large ulcer of the left thigh and knee region, very irregular in shape, involving anterior, posterior, and lateral surfaces. In several places on

the margin there was moderate undermining of the skin; in other places, new skin was growing out from the margin over the granulation tissue. Below the patella there were three sinuses which communicated with one another and entered into the infrapatellar bursa. On the outer side of the thigh there was a long deep groove between the biceps muscle and the bone where the infection had burrowed deeply. There was also an extensive burrowing upward posteriorly from the upper limit of the ulcer, with a large area of indurated tissue beneath the skin. An x-ray film revealed no involvement of the bone or the joint. It was evident that there were portions of the lesion which would require excision, but because of the patient's poor condition, it was decided to be conservative for a time. The whole area was flooded with a creamy suspension of zinc peroxide in distilled water. Fine-meshed gauze soaked in the same material was laid over the surface and packed under the overhanging margins, and the whole area was then sealed with fine-meshed gauze impregnated with zinc oxide ointment. On several occasions large hematomas formed in the superficial layers of

Fig. 43.—(Case 9) Fifteen days after admission, six days after the first skin graft and the partial excision of undermined margins. Note the oval area over the femur where a large superficial hematoma had been lifted off the granulation tissue. The infrapatellar pouch was partly opened by cutting halfway across the patellar tendon. We temporized with the undermining in the popliteal region because of the obvious danger.

the granulation tissue; these were thought to be caused by rubbing but were probably due to a spontaneous bursting of new blood vessels. They did not cause serious trouble, for they could be lifted off without great damage to the underlying tissues. On the ninth day six undermined areas were excised, and the infrapatellar bursa was opened by cutting halfway across the patellar tendon. This did not completely expose the cavity but permitted ready access to it. At the same operation the anterior portion of the wound, except for the recently exposed areas, was covered with about two hundred small skin grafts. These were held in place by a single layer of coarse-meshed gauze sealed to the skin margin with collodion. Saline compresses were applied to the surface and covered with vaseline gauze to prevent evaporation. On the day after the operation a thin suspension of zinc peroxide was applied to the grafted area, and on the next

day, when the coarse-meshed gauze was removed, all but two of the grafts were pink and firmly adherent (Fig. 43). They became fused with each other and with the surrounding skin in short order. On the eleventh day the rest of the anterior and inner portions of the ulcer, as well as the outer side anterior to the groove, between the bone and the biceps muscle, were covered with skin grafts. Two weeks later the rest of the ulcerated area was grafted. Each time the grafts were successful except for one or two which had been placed in the neighborhood of the remaining deep sinuses. These grafts rapidly fused, and the whole area contracted down very satisfactorily, but the infrapatellar pouch and the groove in front of the biceps muscle were slow to heal (Fig. 44). After about a month, however, the infrapatellar pouch closed completely, and the groove showed evidence of contraction. We then decided to begin to get the limb used to a dependent position. Gradually the patient prolonged the period of dependency of the foot at increasing angles. The culture from the groove showed a steady reduction of organisms, and the application of zinc peroxide was stopped for a period of five days with the hope that the wound would

Fig. 44.—(Case 9) Posterior view. Two months after admission. Sinuses persist beneath the biceps muscle and into the popliteal space. Obviously we were not getting satisfactory contact of medication there.

close more rapidly if no more foreign substance was introduced. At the end of this time, however, the patient began to have pain in this region, and on the morning of the sixth day, after he had had his foot on the floor for five minutes every hour, the tissues became swollen, edematous, and discolored. It was evident that the infection was active again in the deep cavity beneath the biceps muscle. The application of zinc peroxide was started again and the leg was elevated, but the groove enlarged and the tissues internal to the biceps muscle in the popliteal space began to swell, indicating that the infection was approaching the surface in this region. The proximity of the popliteal vessels made a radical procedure inadvisable and yet it was obvious that the popliteal space had to be opened and explored. We debated whether to excise a portion of the biceps muscle, but when the incision was made, a cavity was found in the popliteal space surrounding the perineal nerve. This cavity was opened and the roof removed, leaving the peroneal nerve, covered by some granulation tissue, exposed (Fig. 45). The area was cleaned out, as was the infected area beneath the biceps muscle, and although we realized that we had compromised with the

infection by this limited procedure, we felt that the only chance of saving the leg was to attempt to get contact with the infection in this way. Granulations grew up rapidly, and the cultures indicated a rapid diminution in the number of organisms. The space between the peroneal nerve and the biceps muscle filled in partly, but sinuses persisted beneath them. Although the front and inner sides were well healed, on the posterior surface healing came to a standstill, but the amount of drainage was minimal (Figs. 46 and 47).

The culture continued to show the hemolytic streptococcus and *Bacillus pyocyaneus*. On a number of occasions we considered a radical procedure, but then we would be encouraged by a diminution in discharge and the closure of one of the sinus openings. After a sinus had remained closed for two or three days, the region about it would swell, become painful, and have to be opened. A small sinus appeared medial to the internal popliteal nerve, indicating activity of the infection in that region (Fig. 48). This sinus closed on several occasions but opened again, and so it went on for six months, while we hoped against hope

Fig. 45.—(Case 9) Three months after admission. Finally a "conservative radical" operation was performed in which we attempted to lay open the popliteal space, as well as the space beneath the biceps muscle, wide enough for complete contact with the medication. The peroneal nerve surrounded by granulation tissue was also undermined. It may be seen at the lower end of the wound.

that the infection would finally come under control. We realized that the popliteal lymph glands were probably involved and we shrank from the consequences of a radical procedure.

At the end of that time, however, it was evident that we would have to make the effort. The popliteal space was opened, the popliteal artery was found to be surrounded by infected tissue which extended down for a short distance between the bellies of the gastrocnemius muscle. Even though the cavity was opened widely, dressings were excruciatingly painful, and it seemed to be impossible to get contact with every portion of the deep surface. After three or four days the wound began to bleed, and five hemorrhages occurred before we were certain that the popliteal artery had blown out. This of course necessitated amputation, which was done at the junction of the middle and lower thirds through the anterior and lateral grafted skin areas. Cultures at the site of amputation were negative at first, but after two or three days *Bacillus pyocyaneus* appeared. This

caused moderate suppuration of the wound, but the hemolytic streptococcus never came back. On the eleventh day the femoral artery in the stump blew out; the bleeding was promptly stopped by tourniquet and then by a chromic catgut suture. On the next day we ligated the femoral artery below the profunda. A small lymph gland was found directly over the artery, but it was not disturbed, and

Fig. 46.

Fig. 47.

Figs. 46 and 47.—(Case 9) Four months after admission. The inner and anterior surfaces are completely healed. The posterior granulating surface has narrowed, but sinuses still persist beneath the biceps muscle and peroneal nerve and into the popliteal space.

the wound healed without any infection. No further hemorrhages occurred, the wound granulated satisfactorily, and on the nineteenth day was covered with small pinch grafts from the right thigh. All but one of these grafts took, and thereafter the wound rapidly contracted and healed over.

CASE 10.—L. G., aged thirty years. Office patient, first seen Dec. 24, 1935; discharged on May 5, 1936.

History.—This patient came to the office complaining of an ulcer of the right buttock which had persisted for fifteen months. The lesion, which started as a small pimple, had developed into a boil and had gradually increased in size. It had broken and discharged pus for several weeks before it began to take on the appearance of an ulcer, which gradually increased in size until it was about 3 cm. in diameter, with undermined edges. It was excised by his local physician, and the wound closed with suture, but this broke down and the infection continued to spread. Three months later, a more radical operation was done, and the wound was left open. It then began to heal, but healing soon ceased, and for a period of four or five months it remained relatively inert. During this time all sorts of antiseptics were used, and the patient received a great many treatments with the carbon arc lamp. The Wassermann test was negative, the Frei test was negative, and the biopsy of tissue showed no evidence of tuberculosis or malignancy.

Fig. 48.—(Case 9) Eight months after first admission. Wound all healed except for sinuses under the biceps muscle and peroneal nerve and into the popliteal space. It had remained in status quo for three months, then the exudate gradually increased in amount, and a wider dissection of the popliteal space was decided upon. This was followed in ten days by hemorrhage from the popliteal artery, necessitating amputation.

When the patient came to me, the lesion appeared as shown in Fig. 49. There was an oval transverse ulcer on the right buttock, with undermined rolled-in edges and three small perforations in the skin, coming up from the undermined skin flaps. The ulcer measured approximately 1½ cm. in width and 12 cm. in length. Near the inner end was a small daughter ulcer, evidently not connected with the first but similar in character, with undermining of the skin for a distance of ½ cm. or more. The cultures yielded a hemolytic streptococcus which grew better anaerobically than aerobically. The lesion fitted in with the characteristics of the chronic, undermining, burrowing ulcer, but because of the relative limitations of the lesion it was decided to attempt ambulatory treatment. Zinc peroxide was applied in a creamy suspension, and the undermined margins were packed with fine silk ribbon impregnated with the same material and sealed over with vaseline gauze. The patient showed improvement at once. The under-

Fig. 49.—(Case 10) Contamination of a furuncle. On admission, fifteen months after the onset of the disease. Note the rolled-in, undermined skin margins, with daughter ulcers formed both from within and from without.

Fig. 50.—(Case 10) Final healing. This case was treated on an ambulatory basis entirely. The location of the lesion in the gluteal fold made constant contact with the medication impossible. The rolled-in skin margins had to be cut back on four different occasions.

mined skin edges sealed down in certain places, but in others the edges curled under so that the epithelium was in contact with granulation tissue. The margins were therefore cut back so as to expose the deeper portions of the wound. It was difficult to maintain contact when he was up and walking about, and the erect position tended to turn in the skin margins still more, so that healing was slow. He was treated at home by his wife, with occasional visits by the family physician, and he was seen in my office once a week. Healing was rapid when good contact was obtained, but slowed down when the margins rolled in. It was necessary on four occasions to cut back these rolled-in skin margins, but healing progressed steadily, and finally, after four months of ambulatory treatment, the lesion healed (Fig. 50).

SPECIAL FEATURES OF EACH OF THESE CASES WHICH ILLUSTRATE CERTAIN POSSIBILITIES OF THIS DISEASE

In Case 1, the proximity of the sacroiliac joints and the ilia to the original ulcer rendered them particularly susceptible to the invasion of this organism. It is probable that the organism came from the patient's own intestinal tract and was rubbed in by the chafing of the plaster cast. The soft parts responded slowly but, on the whole, satisfactorily to the medication, but the bone, which could not be radically removed, remained infected. It is quite probable that the zinc peroxide used on this patient was not as effective as it should have been. On the other hand, the extensive ramifications of the sinuses in the pelvis may have kept certain portions of the sinuses completely out of reach of the medicine. After the disease had been going on for approximately two years and a half, there was evidence of amyloid degeneration of the internal organs, but the spread of tuberculosis of the lungs was largely responsible for the patient's death. The erysipelas was also a potent factor at the end.

Case 2 illustrates the invasion of an accidental wound by the causative organism. It was accompanied in this case by another anaerobic bacterium which gave the foul odor. This case illustrates also the autoinoculation of the organism into distant areas of the skin, probably by the patient's hands. The undermining of the back of the hand was much more extensive than on the palm, fortunately, and it is possible that the dense mass of the skin of the palm resisted the spread in this direction. It is certain that this case was not treated continuously with effective zinc peroxide. It illustrates how the organism can dig in even in the presence of what seems to be close contact with the medicine and demonstrates also the importance of watching continuously during the course of treatment for such areas of activity. If they appear, they must be given special attention and should be excised before they go very far.

Case 3 illustrates the probable transfer of the infection from one part of the body surface to another. Fortunately, in the axilla the

invasion did not proceed deeply during the course of two years. In the perineal region, however, there were deep sinuses rather than extensive ulcers. This may have been due to the thickness of the skin in these regions. When these sinuses were opened so that close contact with the medication could be assured, they responded favorably. It also demonstrated that it does not save time to temporize with any area however small, where the epithelium has grown beneath a skin flap and lies in contact with granulation tissue. During the healing process this patient developed an irritation of the skin over the hairy portion of the pubis due to an infection of the hair follicles by an accompanying staphylococcus.

Case 4 illustrates the development of multiple daughter ulcers in the neighborhood of the main ulcer by inoculation from without. It illustrates also the extreme danger that exists in cases in which the femoral glands are involved, because of the proximity of the femoral and saphenous veins which may become infected. This case seemed to be under complete control until an ineffective batch of zinc peroxide was used; the infection then spread in the region of the femoral glands, into the deeper tissues, and eventually into the femoral vein, producing a suppurative thrombophlebitis. This is the only case in the series in which the organism was recovered from the blood and produced metastatic lesions. After every operative manipulation there was a sharp fever reaction lasting for several days, and it is quite possible that at such times the organisms might have been recovered if repeated blood cultures had been taken. When a vein becomes thrombosed and an infection invades the clot, it would seem that nothing can stop the spread of the infection except possibly a complete excision of the involved vein, with the probability of an extension further into some of its ramifications even after excision. It was too hazardous to attempt it in this case.

Case 5 illustrates the necessity for wide excision if contact with all of the infected surfaces cannot be obtained conservatively. It also illustrates that the infection can spread down between the muscle layers and resist eradication for a considerable length of time, even with an efficient material. It is quite possible that the frequent attempts at conservative excision did more harm than good; once it is decided to excise, the procedure should be fairly radical, particularly when the infection is spreading down between muscles along fascial planes.

Case 6 particularly illustrates the necessity for complete removal of infected cartilage, and it demonstrates that bone can resist the invasion of the organisms if the infection is reduced to a minimum at the time the bone is exposed to the contamination. This patient was left with a more permanent defect than any of the others because of the loss

of the cartilaginous support of the lower part of the sternum and the fused costal cartilages. It also illustrates the fact that wounds tend to heal slowly if they are constantly moving, and dressings which are sufficiently firm to rub on the surface may erode tender epithelium. It also demonstrates what is frequently seen in untreated cases, namely, that the destruction of tissue in periods of activity of the infection may proceed infinitely more rapidly than the process of repair, and that there is a certain momentum given to the spread of the infection which is difficult to halt even with the application of effective zinc peroxide. This may indicate that at such times the organisms penetrate fairly deeply beneath the surface of the ulcer and are temporarily out of reach.

Case 7 illustrates the fact, as does Case 1, that erysipelas may start and spread from a wound of this type at any time, just as it may from any hemolytic streptococcus infection, and it may recur. In this case infection was in the region of the femoral lymph glands just as it was in Case 4, but fortunately the deep veins did not become involved. There was, however, a tunnel under the gracilis muscle which cleared up by careful application of the medication to the sinus, without radical opening. This should always be tried for a time before a radical procedure is done, which will be mutilative.

Case 8 illustrates the fact that daughter ulcers may be produced either by inoculation of the bacteria from the surface or by undermining beneath the skin. It also shows that the skin can be partially destroyed from beneath but maintain its circulation, and that bridges can be formed with epithelium growing completely around them. Such bridges or skin tabs ought to be removed, for although healing may take place beneath them, it does so slowly, leaving a skin defect which is objectionable. It also illustrates that by persistent care certain deep tunnels may heal without a radical opening, but that this healing is slow, and if a sinus can be opened without too great mutilation of tissues, it will save time in the end to open it early.

Case 9 illustrates how an infection may spread from a trivial abrasion and, in spite of all of the usual methods of surgical treatment, burrow deeply into the subcutaneous tissues and work its way down beneath muscles and involve neighboring lymphatic tissues for a long period of time. The infection in this case burrowed into the infrapatellar bursa but spared the knee joint and the bone. It invaded the popliteal glands, surrounded the popliteal artery and popliteal nerves, and finally perforated the artery but spared the veins. Just when the infection invaded the lymph glands of the popliteal space is uncertain. It may be that a radical dissection of the popliteal space in the early stages of the disease might have saved the leg, but I am inclined to

think that it would have resulted, as it did eventually, in a hemorrhage which would have required disarticulation of the hip joint, with a possible spread up into the pelvic vessels.

The case illustrates the absolute necessity for actual contact with the medication with every part of the infection and the difficulty of controlling the infection in regions where there are lymph glands which have become involved. This case also illustrates the formation of hematomas in the surface layers of granulation tissue and the persistence of *Bacillus pyocyaneus* in the lesion without its being a very important factor in the delay in wound healing.

Case 10 illustrates that this infection may be of low grade and may go on for a long period of time without spreading extensively, but it is characterized by persistency, and its tendency to burrow under the skin causes not only a rolling under of the skin edges, but also multiple perforations of the skin from beneath. I believe that this case was held in check by the large amount of ultraviolet light therapy. This may be due to the fact that the ultraviolet light forms peroxides in the tissue which inhibit, if they do not actually destroy, the organisms.

This case illustrates that certain of these lesions can be controlled under ambulatory treatment if the circumstances require it, but it undoubtedly would have been better to have taken the patient into the hospital where the excision could have been more complete and application with zinc peroxide more satisfactory.

SUMMARY AND CONCLUSIONS

From these cases we may form a composite picture of this disease. It is a chronic infectious process which may occur at any age, in either sex, and on any part of the body surface. It is caused by the invasion of a microaerophilic hemolytic streptococcus which may enter the tissues either through an accidental wound or through an operative wound; or it may invade a lymph gland from a distant source and not produce the lesion at the portal of entry but only after a period of activity within the gland. The lesion is characterized by prolonged suppuration, with the gradual development of an ulcer with undermined, rolled-in skin margins, and sinuses which tend to burrow beneath the skin or into the deeper tissues along lymphatic channels, veins, or fascial planes. The ulcer gradually, but almost irresistibly, enlarges. The base is covered with grayish, gelatinous, anemic, shaggy granulations. Hematomas occasionally form spontaneously in the superficial layers of the granulation tissue. The infection frequently produces daughter ulcers by a perforation of the skin from beneath or by the secondary inoculation of the skin from the surface. If a perforation occurs from within, the daughter ulcer gradually enlarges

and may fuse with the main ulcer or leave a bridge between them, which may become completely surrounded by epithelium on the deep, as well as on the superficial, surface. There is usually a moderate fever and moderate pain in the wound. At times, the temperature may reach 103° F. every day for a period of days, but usually it remains at a lower level. In some cases in which the threshold for sensitivity is low, pain may be intense, and after prolonged illness completely shatter the patient's morale. The infection rarely involves muscle or bone; but when it invades bone, it is almost impossible to eradicate it. The organism rarely invades the blood stream, but occasionally it may be recovered from the blood; and in such cases may produce metastatic foci in other parts of the body. The infection rarely invades the blood vessels, but in long-standing cases it may do so, producing thrombi in them or eroding their walls, causing severe or fatal hemorrhage. In long-standing cases amyloid degeneration of the liver, spleen, and kidneys, may develop. The condition, fortunately, is rare. For this reason, however, it is usually not recognized by any surgeon who sees the case for the first time, and he is likely to treat it as an ordinary infection until its failure to heal makes him realize that he is dealing with an unusual condition. Even then he is not able to make a diagnosis or find out how to treat it successfully because of the meagerness of the literature on this subject. Cases go on for months or years until there is extensive destruction of skin, or a deep penetration resulting in fatal hemorrhage, or the gradual disintegration resulting from amyloid degeneration. Its early diagnosis is therefore of the greatest importance, and this depends not only upon the recognition of the characteristic features of the disease, but also on the early employment of anaerobic methods of cultivation of the bacteria in the wound. In the early stages of the infection the organism is frequently missed because only aerobic cultures have been made, and it is essential that the exudate be planted directly on solid media under anaerobic, as well as aerobic, conditions. It will then be found that the hemolytic streptococcus is uniformly present on the anaerobic plates, and when equal quantities are cultivated aerobically and anaerobically, although a few colonies may be found on the aerobic plates, especially in long-standing cases, it will always be found to grow better anaerobically than aerobically. If colonies from the anaerobic plate are transferred again to plates under both anaerobic and aerobic conditions, certain of those colonies will grow only anaerobically.

It would seem to be of the utmost importance, for the recognition of these cases, to have available bacteriologic laboratories, equipped to do anaerobic bacteriology. This applies not only to this disease but also to many types of chronic and acute surgical infections. It would

be well if the American College of Surgeons would require Class A hospitals to be prepared to do adequate anaerobic bacteriology.

With regard to treatment, every conceivable kind of antiseptic has been used in these cases, without effect. The ingenuity of a great many doctors has been taxed to the utmost in an effort to find some antiseptic which will be effective, but almost all of the antiseptics which have been used have had only temporary effect, and the infection has continued to spread in spite of very careful application of these medicaments. There is some evidence that ultraviolet light has a favorable action in these lesions, for in one case a spontaneous cure was obtained after many months by this method. A number of cases have apparently been benefited and have healed following the use of maggot therapy,[3, 4] but in one of our cases in which this was tried, it had no appreciable beneficial result, and the maggots nearly drove the patient wild by their activity.*

We have demonstrated again and again, however, that the careful application of zinc peroxide will almost invariably effectively halt the spread of this infection. There are certain essential conditions for the success of this treatment. First, the zinc peroxide must be an effective preparation. In other words, it must have certain physical properties which will provide the necessary environment to inhibit or destroy the causative organisms. These physical properties may be determined by a simple laboratory test. Zinc peroxide is a finely divided white powder having the consistency of chalk or talcum. It must be heated at 130° to 140° C. for one to four hours to sterilize it and mobilize the oxygen. When it is suspended in ten parts by weight of distilled water it sediments rapidly, leaving a clear supernatant fluid. In the course of an hour bubbles of oxygen begin to form in the sediment, which after twenty-four hours becomes flocculent and curdy with the evolution of a considerable quantity of oxygen gas. Five grams in 50 c.c. of distilled water should liberate 10 to 20 c.c. of oxygen in twenty-four hours. Further confirmation of the effectiveness of the preparation may be had by determining the amount of soluble oxygen produced in the supernatant fluid and by testing the antiseptic powers of the suspension against the organism which has been recovered from the lesion in any given case.

The next requirement for the successful use of zinc peroxide is that every part of the infected surface must be made available for contact with this medicine. If this is not possible without operation, undermined flaps and sinuses should be widely opened and all of the infected surfaces should be flooded with a creamy suspension of the

*In several cases which have come under observation since submission of this paper, we have used the newly advocated antistreptococcic dye prontonsil or its active principle sulphonamide. Although it is not as active against microaerophilic organisms as against ordinary streptococcus, there is evidence that it may be used in conjunction with zinc peroxide to prevent a spread or recurrence, particularly in those areas which cannot be adequately reached by the zinc peroxide.

powder in distilled water, using approximately equal parts of water and powder. This should not be put on in the form of a paste but in the form of a thick cream, which is able to run to all parts of the wound. The wound should then be packed with fine-meshed gauze or silk ribbon soaked in the same material and sealed with vaseline or zinc oxide gauze to prevent evaporation, drying, crumbling, or caking. This dressing should be removed, the old material and exudate thoroughly washed off with distilled water or saline, and a fresh dressing applied every twenty-four hours. As soon as the undermined flaps have sealed down and new skin has begun to grow in from the margins, the ulcer may be covered with skin grafts of the Reverdin type. These should be held in place with a single layer of coarse-meshed gauze, sealed to the skin margins with collodion, then a dressing of fine-meshed gauze soaked in saline should be applied and sealed over with vaseline gauze to prevent evaporation. After twenty-four hours the saline compresses should be removed, and a thin suspension of zinc peroxide should be applied over the coarse-meshed gauze and sealed in turn with an impermeable covering. Forty-eight hours after the skin graft, the coarse-meshed gauze may be carefully removed, leaving the grafts well supplied with blood. These should all be pink and firmly adherent at that time. Thereafter the grafted area may be flooded daily in the same way as the rest of the wound, with a creamy suspension of zinc peroxide.

If possible, frequent cultures should be taken of various parts of the wound to indicate the presence or absence of the infecting organism. Although clinical evidence of diminished activity is readily recognized, the cultures not only confirm the clinical manifestations but also very often precede them. Under the zinc peroxide treatment, if contact is obtained with every part of the wound surface, the organism rapidly loses its anaerobic predilections, grows as readily aerobically as anaerobically, and very soon loses its hemolytic property on blood agar plates, the colonies taking on a green tinge. Eventually these green progeny of the original organism become permanently green, and although they may resist the bactericidal action of zinc peroxide in the test tube, the wound continues to heal in their presence. The surgeon in charge of the case must be constantly on the lookout for any evidence of reactivity due to failure to obtain contact with some small area difficult to reach. Careful application of the zinc peroxide in such areas will obviate the formation of an active focus, but there is always a possibility of these forming until the area is completely covered with epithelium, and occasionally such areas of reactivity have to be radically excised before they can be completely controlled. When the hemolytic organisms have completely disappeared and the surface is

flat, final epithelialization of the wound may be hastened by the application of an ointment containing 2 per cent oxyquinoline in 5 per cent scarlet red.

This disease should not be confused as Holman[3] has done with the gangrenous type of chronic ulceration which we have previously described in several papers.[5-7] That disease is caused by the synergistic action of a *nonhemolytic* microaerophilic streptococcus which may be found in pure culture in the spreading margin of the lesion, and a *Staphylococcus aureus* which is associated with it in the gangrenous zone which is always present around a part or all of the periphery of the ulcer. That lesion is more superficial. There is no undermining of the skin margins and no sinus formation. The zone of gangrene is surrounded by a raised purple zone, and this in turn by a brilliant zone of erythema.

We have presented herewith ten cases of chronic, undermining, burrowing ulcer caused by a microaerophilic, hemolytic streptococcus, and from these cases have presented a composite picture of this disease. We have outlined the method of treatment with zinc peroxide, which seems to be the only effective method yet devised for stopping the infection and initiating rapid healing of these ulcers. We have emphasized the importance not only of using a preparation of this chemical, which has certain necessary physical properties which can be tested in any laboratory, but also the necessity for meticulous care in the correct application of the medication, and we have indicated other steps in the technic which favor the eventual healing of the wound. An urgent plea is made for the early recognition of these cases and also for the establishment of adequate facilities in every hospital for anaerobic bacteriologic service.

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COMPLETE COMPOUND COMMINUTED FRACTURE-DISLOCATION OF THE ASTRAGALUS

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COMPLETE dislocation, simple or compound, of the astragalus is a rare injury. A compound comminuted fracture-dislocation of this bone is seldom seen. The astragalus may be dislocated in any one of five positions: medial, lateral, anterior, posterior, or rotary. The mechanism of the dislocation is little understood, except that it takes severe violence to produce a complete dislocation.

At one time the treatment advocated for this type of injury was excision of the astragalus, as it was thought that after its complete dislocation the circulation was so severely impaired that necrosis would follow any type of reduction.

The circulation of the astragalus has been little understood, as very little investigative work has been done along this line; but Sneed[1] has presented an excellent study of the blood supply of the astragalus. It is one of the few studies of its kind to be found in the literature.

In the simple dislocations of the astragalus there is a marked deformity. The dislocated bone may be seen and palpated under the tightly stretched skin. The malleoli and os calcis are usually uninjured; the malleoli generally rest on the os calcis. Radiographs should be taken to confirm the diagnosis.

Simple dislocations should be reduced immediately by closed reduction under a general anesthetic. It may sometimes be necessary to use a pin through the os calcis in order to obtain the proper amount of traction. While traction and countertraction are maintained, the astragalus is forced back into its normal position by direct pressure. If this is impossible, open reduction should be employed.

Sneed[1] reported a most interesting case, in which open reduction was necessary, the peroneal tendons had to be cut, and the astragalus was completely removed, after which the bone was replaced. The result was excellent, and there was no change due to any interference with the blood supply.

Compound dislocations occur occasionally and should be treated according to the principles of treatment of any compound dislocation. The bone may be fractured, but even in this instance, notwithstanding the fact that it is comminuted, reapposition of the fragments and replacement of the bone should be done if possible. The following case will illustrate recovery from this type of injury.

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CASE REPORT

D. L., colored male, aged fifty-four years, was admitted to the Employees' Hospital, July 29, 1935, shortly after he had sustained a severe injury to his right ankle while working in a coal mine. The patient stated upon admission to the hospital that he had been struck on the right shoulder by a large rock, which fell from above. This knocked him down, and another rock fell on his right foot and ankle, causing a serious open wound in the region of his ankle.

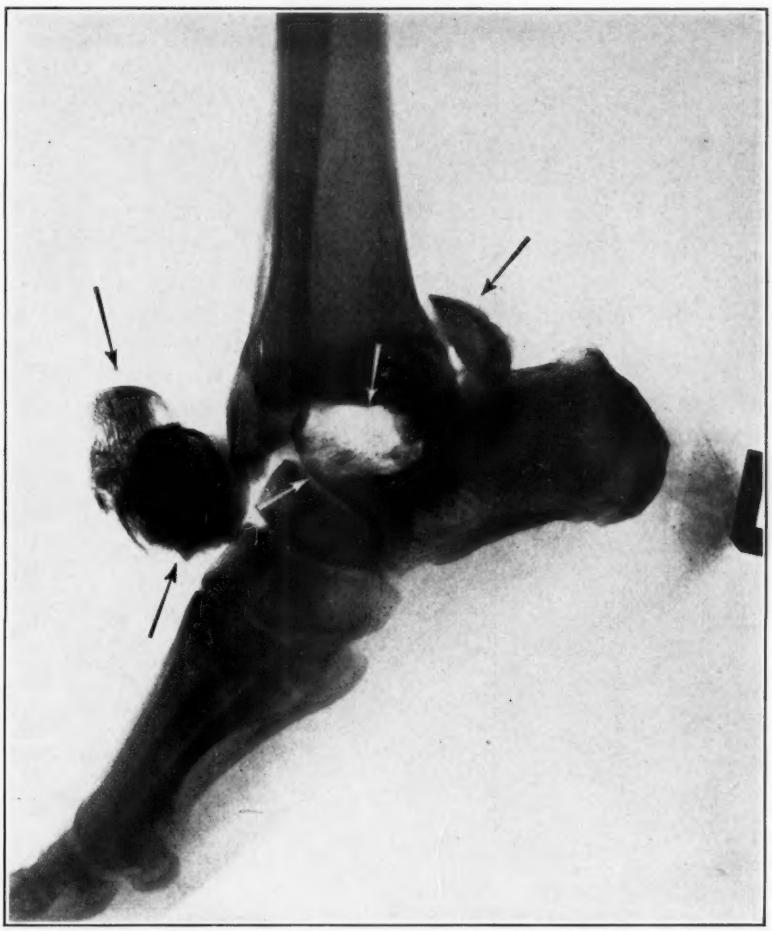

Fig. 1.—A compound comminuted fracture-dislocation of the right astragalus, fragments being displaced, anteriorly, posteriorly, and laterally.

Examination on admission to the hospital revealed a well-developed and nourished negro male. He was in severe pain, complaining of discomfort in the right shoulder, chest, and ankle. Patient was moderately shocked. Examination of the right ankle revealed an extensive compound comminuted fracture-dislocation of the astragalus. It was completely severed from all its attachments except for a few fibers of the external lateral ligament of the ankle. There was a laceration on the outer aspect of the ankle, about three inches in length, which opened up the entire ankle joint, and through which the astragalus protruded. The entire wound was contaminated with particles of dirt, rock, and coal. Active hemorrhage was present.

A roentgenogram revealed a comminuted fracture-dislocation of the astragalus (Fig. 1). The astragalar fragments were displaced outwardly, anteriorly, and posteriorly. Following the treatment for shock, the patient was taken to the operating room, and under general anesthetic, the wound was thoroughly cleansed and débrided. The astragalus was so severely comminuted, being torn almost entirely from its ligaments, that a complete astragalectomy was at first considered the only possible treatment. After the wound was cleansed and débrided, however, attempts

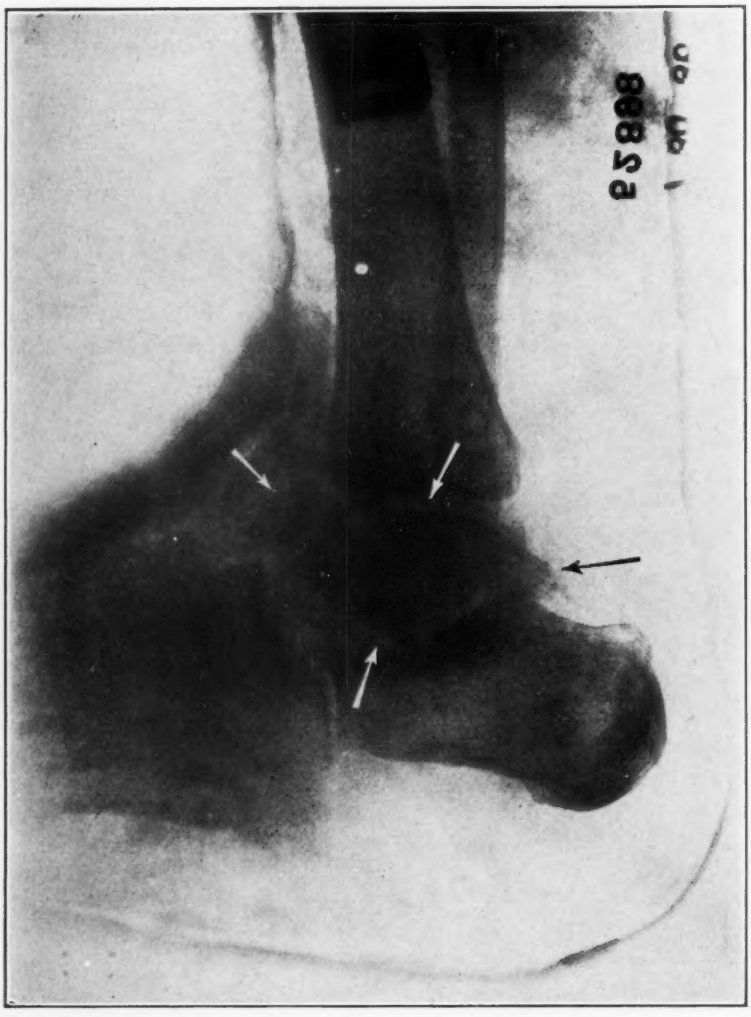

Fig. 2.—Position of the astragalus following reduction. Because of the marked comminution, it was impossible to replace all fragments in perfect position.

were made to get the fragments of the astragalus into reapposition and replace them in their original site in the tibiofibular mortise. This was done with difficulty, but it was decided that the wound would be closed without performing an astragalectomy, even though there would be considerable danger of necrosis of the astragalus due to a possible loss of circulation. The wound was closed without drainage. A circular plaster cast was applied to the foot and leg above the knee, with the knee in slight flexion. A window was cut in the cast for observation and care of the wound. Healing occurred by primary intention.

Roentgenogram taken immediately after reduction of the dislocation showed that there was not an accurate anatomical reduction (Fig. 2), but due to the severe comminution, it was thought this position could hardly be improved upon.

The cast was removed after a month, when the wound had healed and the swelling had practically subsided. Another cast was applied from the base of the toes to the middle of the thigh, and the patient was allowed to be out of bed with crutches. This cast was removed in two weeks, and a light cast was applied to the foot and leg below the knee, which was removed two weeks later or two months after injury.

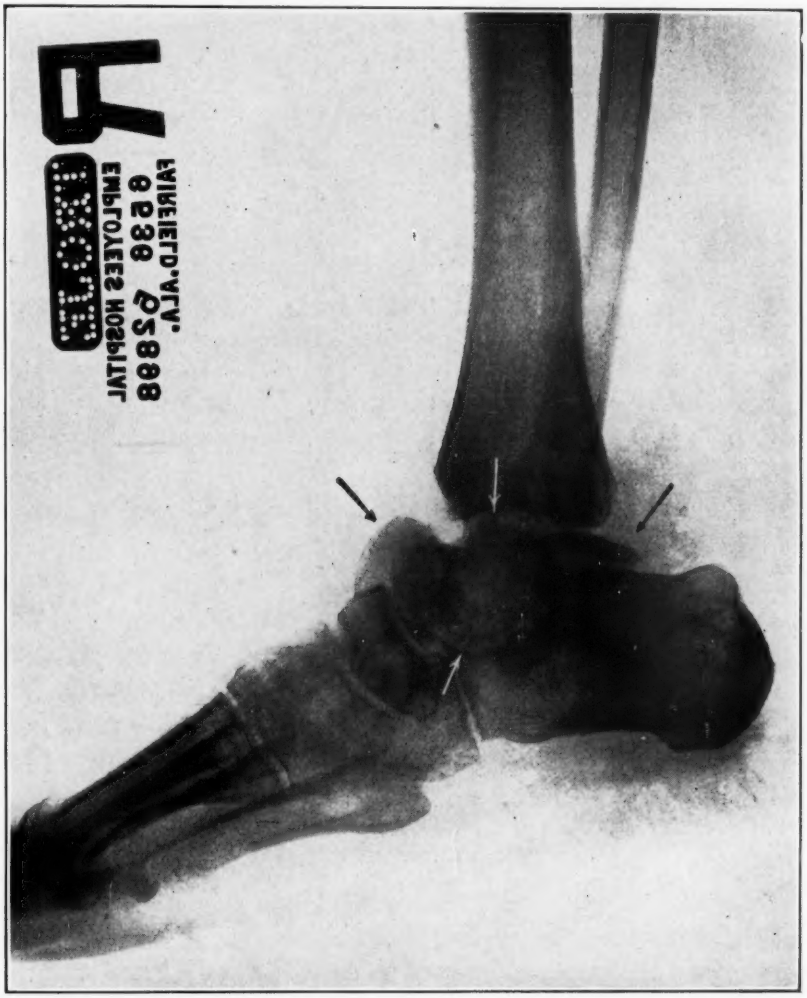

Fig. 3.—Roentgenogram, taken ten months after injury, shows no necrosis. Even though the position of fragments are not perfect, the weight-bearing surface and alignment are good, much better than if no astragalus was present.

Weight-bearing, with the aid of crutches and an ankle and leg brace, was started three months after injury. The crutches were discarded a month later. The ankle continued to swell considerably on active weight-bearing, but this slowly subsided, and the patient could walk without pain or discomfort.

Roentgenogram (Fig. 3) taken ten months after injury revealed no necrosis of the astragalus.

The patient was last seen on May 22, 1936, for follow-up. At that time there was still slight enlargement of the right ankle joint, with only moderate limitation of motion. The patient walked without ankle or leg supports, and even though there was a slight limp, he was free of pain (Fig. 4*A* and *B*).

Fig. 4*A*.

Fig. 4*B*.

Fig. 4, *A* and *B*.—Photographs showing the condition of the foot and ankle ten months after injury.

COMMENT

The results obtained in this case, although accurate anatomical reduction was impossible, seem to justify replacement of the astragalus, even when there is a compound comminuted fracture-dislocation of the bone. It is interesting to note that in this case there was evidently serious circulatory disturbance in the bone which reestablished itself without the occurrence of any necrosis.

SUMMARY AND DISCUSSION

1. Complete dislocations of the astragalus are unusual. Compound comminuted fracture-dislocations of the astragalus seldom occur.

2. Immediate closed reduction is the treatment of choice in simple dislocations and is usually successful.

3. Open reduction is indicated at once if the closed method is unsuccessful.

4. Compound dislocations, with or without fractures, should be treated by cleansing and débridement of the wound and a replacement of the dislocated bone.

5. The circulation is usually reestablished in the astragalus, even though it is severed from all connections.

6. A case of compound comminuted fracture-dislocation of the astragalus is reported in which reduction was performed without the occurrence of necrosis, and the functional result was satisfactory.

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THE OPERATIVE TREATMENT OF HYDRONEPHROSIS DUE TO OBSTRUCTION AT THE URETERO-PELVIC JUNCTION*

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HYDRONEPHROSIS due to obstructive lesions at the junction between the renal pelvis and the ureter is a relatively common condition, 25 cases having been seen at the University Hospital since April, 1930. Its frequency is probably due to the variety of lesions which may produce it. The causative lesions are best classified as follows:

1. Fibrosis in the wall of the ureter (stricture).
2. Fibrosis about the ureter (compression, angulation).
3. Accessory vessels to the lower pole of the kidney, if accompanied by periureteral adhesions or by nephroptosis.
4. Neurogenic dysfunction of the pelvis and ureter.
5. High (nondependent) attachment of the ureter to the renal pelvis.

THE MECHANISM OF OBSTRUCTION

The mechanism by which these conditions produce hydronephrosis may vary considerably. Fibrosis, either inflammatory or traumatic, may produce a ureteral stricture (Fig. 1, *a*) or, by infiltrating the wall of the ureter, render it inelastic and so impede peristalsis as to cause stasis, without actually compromising the lumen of the ureter. Periureteral fibrosis is probably not important unless it also invades the wall of the ureter or kinks it very sharply while binding it to adjacent structures, such as the renal pelvis, the posterior abdominal wall, or accessory renal vessels (Fig. 1, *b*). Kinking of the ureter without infiltration or fixation does not cause obstruction.

Whether accessory renal vessels unaccompanied by any other abnormality may interfere with drainage of the renal pelvis is open to grave doubt, although Quinby claims that the continual pounding of an artery against the ureter may disturb peristalsis sufficiently to produce hydronephrosis. Fibrosis about the ureter and accessory vessel (Fig. 1, *b* and *c*), or an associated ptosis of the kidney, may undoubtedly lead to compression of the junction by the vessel.

In a few cases of hydronephrosis without dilatation of the ureter, it is necessary, because of the absence of any demonstrable pathologic state, to assume a defect, presumably neurogenic, in the activity of the pelvic and ureteral muscle. This may take the form of a spasm of the circular

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muscle at the junction, or of peristalsis too feeble to empty the pelvis. Many of these cases are probably actually due to an unrecognized mechanical obstruction.

High insertion of the ureter or, more properly, high attachment of the ureter to the renal pelvis, is often mentioned as a cause of hydronephrosis, the latter being attributed by Fenger to the formation between the pelvis and ureter of a valve which is closed by a rise in the intrapelvic pressure (Fig. 1, *b* and *c*). More probably the high position of the ureteropelvic junction is secondary to the dilatation of the pelvis incident to one of the causes already enumerated.

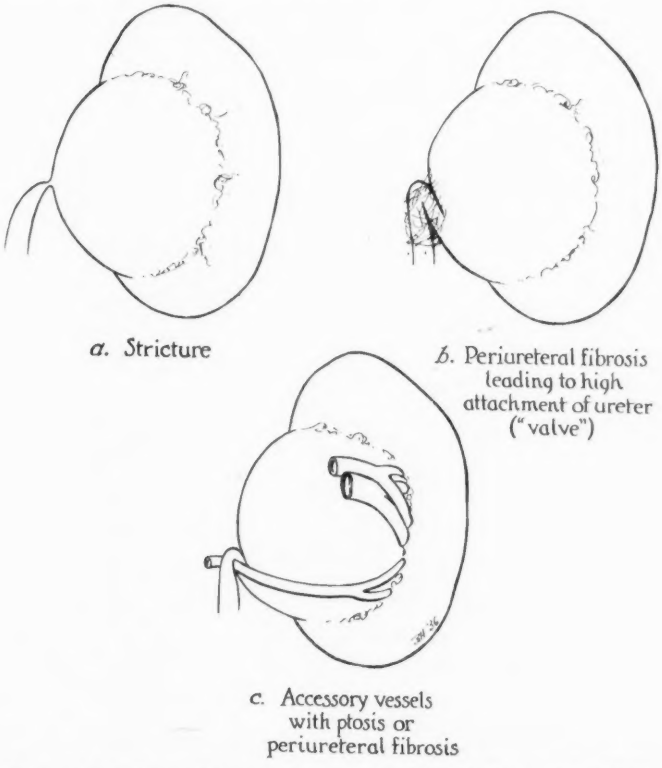

a. Stricture
b. Periureteral fibrosis leading to high attachment of ureter ("valve")
c. Accessory vessels with ptosis or periureteral fibrosis

Fig. 1.—The chief lesions which produce obstruction at the ureteropelvic junction.

THE CLINICAL PICTURE

The clinical appearance of these conditions is variable, and may consist of an occasional vague pain in the flank, intermittent or continuous renal pain or colic, attacks of recurrent acute infection, chronic pyuria, or of reflex gastrointestinal disturbances without pain. The classical picture of Dietl's crisis (polyuria following colic), is rarely seen. It is worth remembering that the urine is often normal, and that, in an occasional case, the symptoms are all, or nearly all, gastrointestinal in character.

There are no constant physical findings, although the affected kidney may be palpable during attacks. Fever is usually dependent upon in-

fection, and the picture of recurrent acute pyelonephritis in young people is that most often seen.

The diagnosis is dependent upon pyelography. Usually the excretory urogram suffices, but a retrograde pyeloureterogram is often required to demonstrate that the ureter below the obstruction is normal, since the latter often prevents filling of the ureter during excretory urography. The pyelogram ordinarily shows a hydronephrosis, with a ureter of normal caliber. Certain other changes are suggestive when present; namely, a bifid renal pelvis, a squared pelvic outline, and a high attachment of the ureter to the renal pelvis.

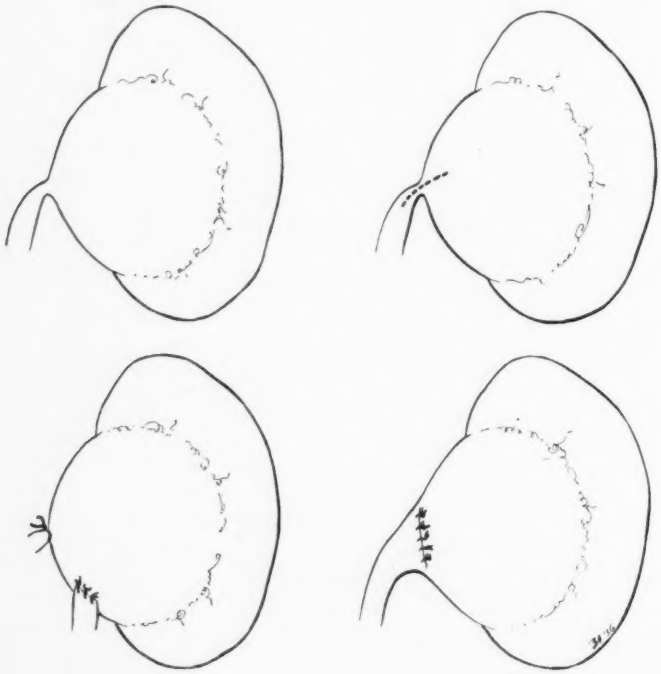


Fig. 24.—The operations for obstruction at the ureteropelvic junction.

TREATMENT

Unfortunately, the majority of these cases are treated by nephrectomy (fifteen cases in this series). There are several reasons for this. The patient may fail to seek advice until the kidney is too completely disorganized to permit saving it, although, in my experience, a kidney containing as little as one-third of the normal amount of parenchyma may be reclaimed. Conservative operations upon such kidneys are amply justified by their results, and by repeated experimental observations showing that animals may survive when two-thirds of their total renal parenchyma has been removed (and seven-eighths if small portions of

the kidney are removed in stages, allowing hypertrophy to follow the removal of each bit before proceeding further).

Many surgeons are unaware of the possibilities of conservative operations upon the kidney, while others oppose them except in bilateral disease, agreeing with Hinman that, if the kidney opposite to the lesion has undergone hypertrophy, the affected one will atrophy in spite of attempts to save it. Hinman argues that the presence of the hypertrophied normal kidney prevents the stimulus to function from reaching the damaged organ. While this view is borne out by Hinman's experiments, it has been repeatedly disproved in practice, particularly by

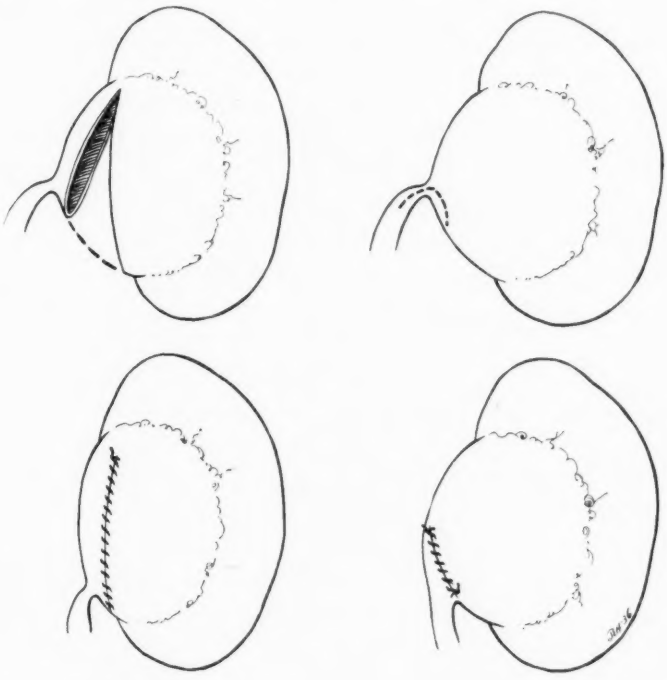


Fig. 2*B*.—Operations for obstruction at the ureteropelvic junction.

the experiences of Bazy, Legueu, von Lichtenberg, and Wildbolz. They have reported instances in which the kidney functioned normally or was normal anatomically fifteen to twenty-four years after conservative operations for hydronephrosis due to obstruction at the outlet of the renal pelvis.

With the possible exception of an occasional stricture at the ureteropelvic junction, nonoperative measures are of decidedly limited value. They consist of the administration of urinary antiseptics, of ureteral dilatation, and of lavage of the renal pelvis. Recurrence is the rule after such treatment, and the condition is often aggravated by it.

All forms of operative therapy (Figs. 2 and 3) have as their object the relief of stasis in the renal pelvis, with reduction in the size of the pelvis as a secondary and less important consideration, although the latter is desirable if the pelvis is very large, in which case its size renders peristalsis ineffective.

The first deliberate conservative operation for obstruction at the ureteropelvic junction was probably that of Küster (1892), who, in the presence of a hydronephrosis due to a stricture at the junction, ligated the ureter, cut it off below the stricture, and reimplanted it into the dependent portion of the pelvis. The patient recovered. The method is still rather widely used, notably by von Lichtenberg, Wildbolz, and

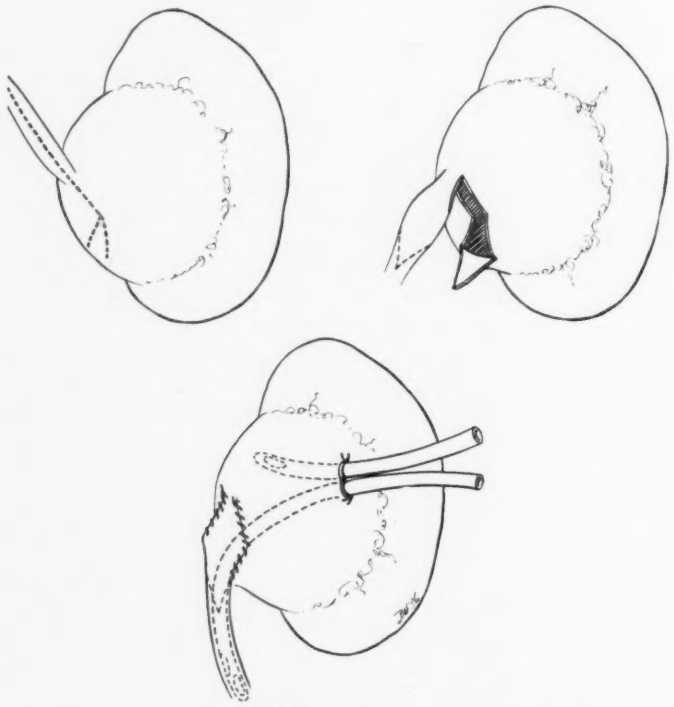


Fig. 3.—Y-plasty (Foley).

Quinby. The possibility of a recurrent stricture at the point of anastomosis constitutes a theoretical objection to the operation. Another defect in this method is that it interrupts the continuity of the ureter with the pelvis, which is undesirable if it be true that peristaltic waves originate in the pelvis and pass down the ureter.

Next in point of time is the operation of Fenger (1894) who incised the stricture longitudinally and closed it transversely. This operation has many advocates, but Herbst and Polkey have shown experimentally that it produces a kink in the ureter opposite the suture line, and that this kink may itself produce obstruction and so defeat the purpose of the operation.

When the ureter is angulated and plastered against the pelvis, von Lichtenberg has made a lateral anastomosis between them, based on the Finney pyloroplasty. The method has been used successfully by Walters. It has the objectionable feature that the spur formed between the ureter and pelvis may become edematous and cause obstruction.

Gayet has advocated resection of the redundant pelvis in such a manner as to place the ureter in a dependent position, but this operation fails to correct the obstruction, which Gayet assumed to be due to the high attachment of the ureter. Young has attempted to overcome this fault by adding Fenger's plastic operation, the objections to which have already been noted.

When the obstructing force appears to be an anomalous blood vessel, Hellström resects the excess pelvis and sutures the vessels to the pelvic wall above its connection to the ureter.

In a similar situation Patch severs the pelvis transversely above the level of the anomalous vessels, and resutures it on the other side of them.

I do not believe that anomalous blood vessels cause hydronephrosis unless the ureter is angulated and fixed around them by periureteral fibrosis or nephroptosis, and I prefer, in such cases, to widen the ureteropelvic junction on the assumption that spasm or anatomic obstruction exists. Moreover, ligation of a renal vessel invariably produces infarction of the area supplied by it. While this is usually a silent process which destroys only a small portion of the kidney, it may become infected and necessitate nephrectomy.

Alleman has advocated longitudinal incision of the circular muscle at the junction down to, but not through, the mucosa for those cases seemingly due to spasm, as in the Fredet-Rammstedt operation for pyloric stenosis, but this method, like divulsion of the junction with a bougie at operation, seems to invite recurrence.

To my mind the most satisfactory method of dealing with these cases is the operation devised by Schwyzer and improved by Foley (Fig. 3).

Schwyzer divided the posterior surface of the upper inch of the ureter by a longitudinal incision, which he then prolonged upward onto the pelvis in the form of a V. The apex of the triangular flap of pelvic wall thus outlined was pulled down to the lower end of the incision in the ureter, and the incision closed as a V, thus widening the junction without interrupting its continuity or angulating it.

Foley has moved the longitudinal incision in the ureter onto its lateral aspect, and extended it above the ureteropelvic junction. One limb of the V incision in the pelvis is placed on its anterior, and the other on its posterior surface, so that suture places the junction in a dependent position. The V-shaped closure is made by carefully placed interrupted sutures of 0000 chromic catgut on atraumatic needles. These sutures include only the muscularis and adventitia, and do not penetrate the mucosa. A small catheter is placed through the anastomosis and brought out through the posterior surface of the pelvis. Openings into the

catheter are so placed that it drains the pelvis, diverts the urine, and splints the anastomosis during healing. More recently Foley has employed an additional catheter as a pyelostomy. Three painful experiences caused by slipping of such tubes, with consequent extravasation of urine into the wound, have led me to supplement the diversion of the urine by inserting a No. 22 Malecot catheter into a lower calyx of the kidney as a nephrostomy.

Foley has placed considerable emphasis on the importance of nephropexy, but I have purposely avoided high fixation of the kidney. I have simply held it high enough to avoid kinking of the ureter by suturing the perirenal fat and peritoneum loosely beneath the lower pole of the kidney, somewhat in the manner of Deming. The results have convinced me that a painstaking nephropexy merely adds unnecessarily to the length of the operation.

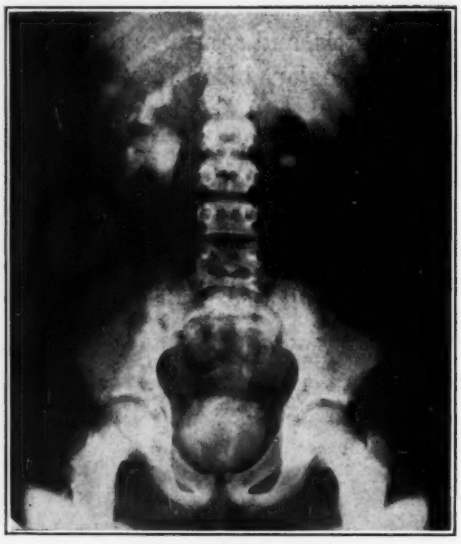


Fig. 4.—Hydronephrosis before Y-plasty (Case 1).

THE RESULTS OF OPERATION

I have performed this operation nine times, supplementing it twice by excision of redundant pelvic wall, and once by resection of the lower pole of the kidney, together with a contained stone which could not be located. In an additional case, Küster's division of the ureter with reimplantation into the dependent portion of the pelvis was done, and supplemented by excision of most of the wall of the pelvis.

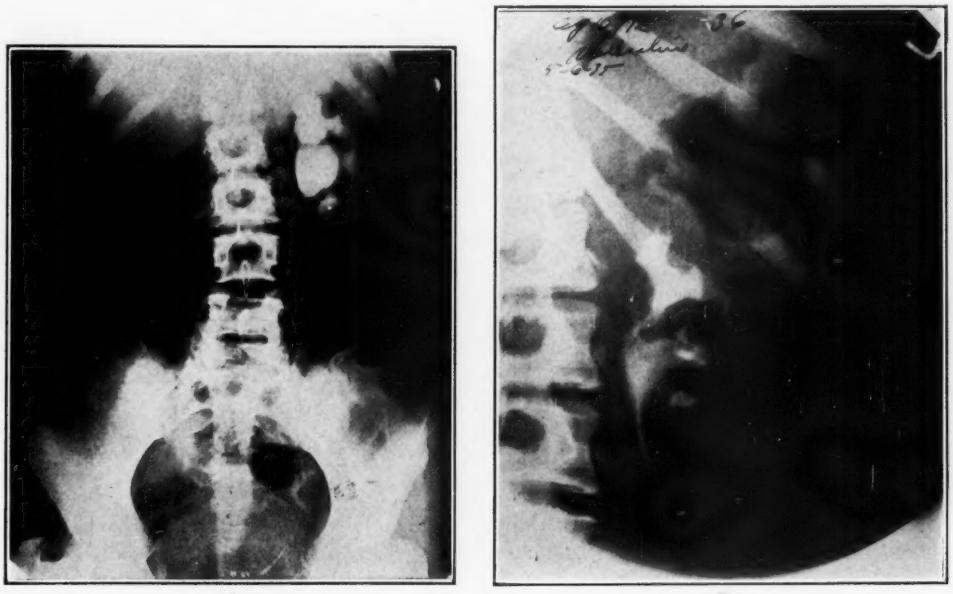
The first operation was done in November, 1932, the last in June, 1936. The patients ranged in age from ten to fifty-seven years. There were no deaths. Several presented postoperative complications, but all have recovered and are entirely symptom-free at the present time, with the exception of one patient who required nephrectomy ten weeks after operation because of persisting obstruction and extravasation of urine. All patients operated upon more than six months ago have had pyelo-

grams made at least six months, and in one instance three years, after operation, which show functioning kidneys secreting clear, uninfected urine. In all but one there has been a notable reduction in the size of the pelvis since operation; in the one in which the size of the pelvis has remained unchanged (Fig. 4) an infection of four years' standing has disappeared, together with all symptoms.

COMPLICATIONS

Complications of varying severity followed operation in 5 cases.

In the first of these, a thirteen-year-old boy, an accessory vessel to the lower pole was divided, a large portion of the pelvis was resected, and the ureter was reimplanted into a dependent position. A temperature of



A. *B.*

Fig. 5.—Hydronephrosis (*A*) before and (*B*) after Y-plasty and partial resection of pelvis (Case 4).

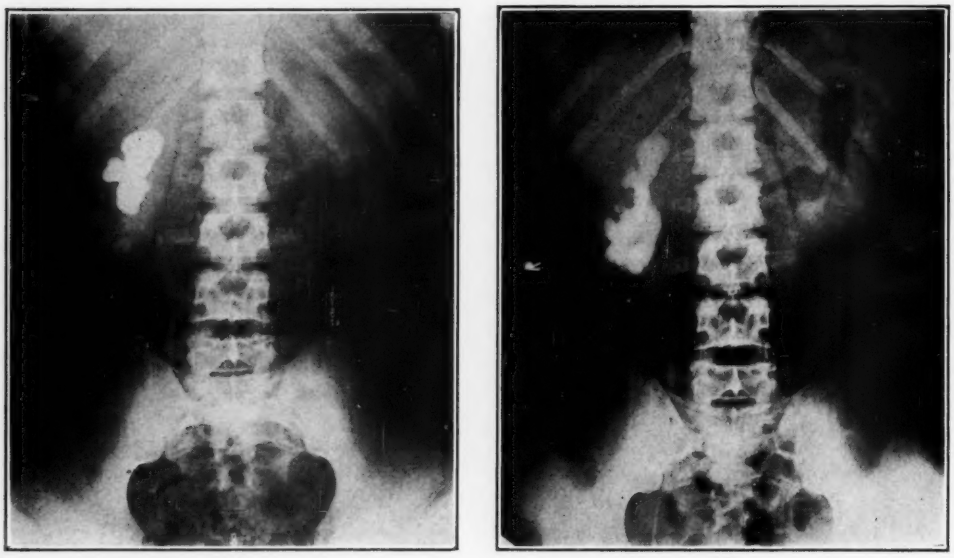
105° F., without subjective or objective findings, appeared on the third day and lasted three days, apparently from infarction of the lower pole of the kidney. Thereafter recovery was normal. One and one-half years later the patient was well, the preoperative infection had disappeared, and the kidney functioned well as judged by excretory urography, considering that only one-third of the normal amount of renal parenchyma was present at operation.

In the second, a man twenty-five years old, a pseudoleucemia followed operation, the white blood count rising to 47,000 and the hemoglobin falling from 90 to 40 without evidence of hemorrhage. This reaction subsided uneventfully following transfusion. A year later the urine from the right kidney was clear, and retrograde pyelography disclosed a very marked reduction in the size of the renal pelvis.

In the third instance, colic in the unoperated kidney occurred when the patient got up after operation (resection of the lower pole of the right kidney with an enclosed stone, Y-plasty); a stone was subsequently passed from the left side. Retrograde pyelography eighteen months after operation disclosed a considerable reduction in the size of the kidney, which secreted clear urine.

In the fourth, a woman of thirty-five, urine was discharged through the incision for ten weeks after operation; at cystoscopy a piece of necrotic tissue was seen protruding from the ureteral meatus. Closure of the fistula followed extraction of the necrotic tissue and ureteral dilatation.

In the fifth patient, a woman of thirty, operation was a failure due to a technical blunder. She had a stricture at the ureteropelvic junction, another in the upper third of the ureter, and a third at the upper



A. *B.*

Fig. 6.—Hydronephrosis (*A*) before and (*B*) after Y-plasty and resection of the lower pole of the kidney (Case 3).

margin of the sacrum. Repeated ureteral dilatations having proved fruitless, Y-plasties were done on the upper two strictures and a nephrostomy was made with a plain catheter, the intention being to repair the third stricture later. An extravasation of urine followed slipping of the tube, and nephrectomy had to be done some months later for a renal fistula.

SUMMARY AND CONCLUSIONS

1. Obstruction at the ureteropelvic junction may be due to stricture, to compression by scar tissue, to anomalous vessels to the lower pole of the kidney complicated by periureteral adhesions or by nephroptosis, and to disturbances of the nervous mechanism of the ureteropelvic junction, leading to ineffective peristalsis or to spasm.

2. Nonoperative treatment is of very limited value, its effects being purely palliative.

3. The various operations designed to correct obstruction at the ureteropelvic junction have been described.

4. The Y-plasty of Schwyzer and Foley is, in my opinion, the method of choice, in that it widens the ureteropelvic junction without interrupting its continuity or producing angulation or spurs.

5. Ten cases are reported, in 9 of which Y-plasty was done. In 2 of these, redundant pelvic wall was also resected, and in 1 the lower pole of the kidney was removed, together with a contained stone.

6. In the tenth case, the ureter was divided and reimplanted into a dependent position, and the redundant pelvis was resected.

7. In one case, an infected infarct followed ligation of vessels to the lower pole but did not impair the end-result.

8. There was no mortality. All patients except one have been relieved of all symptoms, and all infections have subsided.

9. Nephrectomy was later required in one case because of persisting obstruction with urinary extravasation.

10. There is a wide field for this type of operation.

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THE EFFECTS OF URETERAL OCCLUSION ON THE BLOOD FLOW AND OXYGEN CONSUMPTION OF THE KIDNEYS OF UNANESTHETIZED DOGS

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A METHOD was described recently by Mason, Blalock, and Harrison[1A, 1B] which enables one to determine directly the flow of blood through the kidneys, and which also permits one to obtain renal venous blood for analysis in unanesthetized dogs. The present publication deals with the results of the application of this method to the study of the circulation through the kidneys following ureteral obstruction.

METHOD

Dogs were employed as experimental animals. They were trained to lie quietly upon the table. No anesthetic was used except for the local injection of novocain over the external jugular vein at the site where a cannula was to be introduced. The animals exhibited no evidence of pain during the course of the experiments.

The principle of the method consists of producing a temporary blockage of the inferior vena cava both above and below the entrances of the renal veins, and diverting the blood during this brief period into a cannula which has been passed into the inferior cava through the external jugular vein. The cannula was 45 cm. in length and was made of brass. The distal end (kidney) was closed, and the proximal end (neck) was patent. The cannula was equipped with two externally expanding balloons, one located at the distal end, and the second 7.5 cm. above it. These could be inflated with air from the proximal end of the cannula through two fine tubes lying in its lumen. Multiple perforations into the lumen of the cannula were present between the balloons. The balloons were inflated only during the time that the blood was allowed to flow from a rubber tube which was attached to the proximal end of the cannula. The level at which the outflow tube was placed has been discussed.[2] The length of time that was required for the escape of 50 c.c. of blood was determined, the blood being replaced immediately following the measurement. The sample of

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renal venous blood for analysis was obtained from the cannula, and the arterial blood was taken from the femoral artery. Heparin was used as the anticoagulant.

A preliminary operation was performed under general anesthesia approximately one week before carrying out the control determinations on the renal blood flow and oxygen consumption. At the time of this operation, all visible veins which entered the renals or the inferior vena for a distance of 3 cm. above and below the level of the renals were ligated. The one exception was the right adrenal vein which was occluded distal to its entrance into the gland, but which was free to convey blood from the adrenal to the vena cava. The second purpose of the operation was to locate the position of the entrances of the renal veins with respect to a scar on the anterior abdominal wall, in order that the cannula could be passed subsequently to the correct point.

The control determinations were performed approximately one week after the preliminary operation. After a second interval of about seven days, each ureter was occluded by a heavy tape ligature at a distance of several centimeters from the entrance into the bladder. The ureter was doubly ligated with silk between the tape and the bladder, and it was divided between the ligatures. In one experiment, obstruction of the urinary tract was produced by occluding the base of the bladder with a heavy ligature of tape. The animals were observed carefully, and further measurements of the renal flow were made when they began to show signs of uremia. This was usually on the third or fourth day following the occlusion of the ureters.

RESULTS

The data of eight consecutive experiments are given in Table I. Eleven experiments were performed prior to the eight which are described in the table, but the results will not be given in detail for the following reasons: In some instances, the ligatures had cut through one or both ureters, and urine was present in the peritoneal cavity. In several experiments, the condition of the animal was so poor that shock undoubtedly was complicating the observation. In addition, the animals became quite anemic in some of the earlier experiments, and a proper evaluation of the results was difficult. There is one striking point, however, in the results of these eleven studies as well as in those described in the table, and that is the fact that the arteriovenous oxygen difference is small in most instances. This applies to the determinations before and after occlusion of the ureter. One additional point deserves comment. It was found in one experiment that the renal blood flow three days following occlusion of the ureters was

TABLE I

THE EFFECTS OF URETERAL OBSTRUCTION ON THE RENAL BLOOD FLOW AND OXYGEN CONSUMPTION

DOG NO.	DATE	WEIGHT KG.	LENGTH CM.	ARTERIAL BLOOD PRESSURE MM. HG			NPN	OXYGEN CONTENT VOLS. PER CENT		A. V. DIF. O_2	RENAL BLOOD FLOW. C.C. PER MIN.		O_2 CONSUMPTION. C.C. PER MIN.		REMARKS
				BEFORE LIGATION	BEFORE STUDY	AFTER STUDY		ARTERIAL	TUBE		TOTAL	PER KG.	KIDNEYS	PER GM. KIDNEY	
128	8/22	10.4	86.5		124			16.56	13.95	2.61	203	19.5	5.3	.059	
	8/22	10.4	86.5		124			15.88	13.82	2.06	219	21.1	4.5	.050	
	9/ 9	10.45	86.5	130	170	138	150	15.32	10.42	4.90	169	16.2	8.3	.093	4-day obstruction. Kidneys 89.5 gm.
3	8/28	17.7	96.0					16.67	14.14	2.53	333	18.8	8.3	.052	
	9/11	17.35	97.0	120	135		133	13.17	10.27	2.90	250	14.4	7.2	.046	3-day obstruction.
	9/12	17.4	97.0	120	130		171	12.91	10.56	2.35	265	15.2	6.1	.039	4-day obstruction. Kidneys 158.2 gm.
29	8/26	15.03	94.0								319	21.2			Toronto Heparin.
	9/14	12.65	95.0	116	130	138	200	12.23	9.99	2.24	221	17.5	4.95	.032	3-day obstruction. Kidneys 156.3.
31	8/29	16.71	97.0					16.57	11.90	4.67	365	21.8	17.05	.108	
	9/15	15.96	99.0	118	124	128	133	15.12	12.98	2.14	184	11.5	3.94	.025	3-day obstruction.
	9/16	15.5	99.0	118	118	126	200	15.50	13.97	1.53	210	13.6	3.21	.020	4-day obstruction. Kidneys 157.1 gm.
27	8/31	14.8	91.0					16.78	13.60	3.18	263	17.5	8.36	.077	
	9/17	13.38	91.0	124	112	98	200	16.95	14.66	2.29	155	11.6	3.55	.033	3-day obstruction. Died following day. Kidneys 108 gm.
34	9/ 2	14.2	91.0								235	16.5			
	9/23	14.1	91.0	135	160		35	16.93	15.30	1.63	117	8.3	1.91		5-day hydronephrosis, bladder ligation.
36	9/18	10.56	79.0								283	26.80			
	10/ 2	10.1	79.0		190		200				200	19.80			4-day obstruction.
	10/ 3	10.0			210	170	240				167	16.7			5-day obstruction. Kidneys 101.5 gm.
195	9/25	10.8	83.5								361	33.42			
	10/ 6	9.7	82.5	135	135	142	250	9.26	6.86	2.40	123	12.68	2.95	.027	4-day obstruction. Kidneys 111 gm.

the same as it had been in the control studies. At autopsy it was found that both ureters were draining into the peritoneal cavity as a result of the cutting through of the ligatures.

DISCUSSION

There was a reduction in renal blood flow in each of the eight experiments. The percentage reduction in flow varied from 23 to 66 per cent in the different experiments, the average being 41 per cent. The difference in oxygen content of the arterial and renal venous blood was small in most experiments, both before and after ureteral ligation. In one experiment (No. 31), the arteriovenous difference was high in the control study; and in another experiment (No. 128), it was high following obstruction of the ureters. We doubt the correctness of these results. It has been pointed out previously that the figures for blood flow are probably more nearly correct than those for oxygen consumption. This is due to the fact that oxygen content of renal venous blood is high as compared with that of neighboring structures, and a slight error in collection may make a significant alteration in the figure for oxygen consumption without changing greatly the true value for the renal blood flow.

The hydronephrosis which resulted from the ligation of the ureters was not very marked in any of the studies. The duration of life following such a procedure is not sufficiently long to permit an extensive change to take place. However, the ureters were dilated, the pelves of the kidneys were dilated, and the nonprotein nitrogen content of the blood was elevated. At any rate, we were interested in studying the early effects of acute obstruction and not the chronic stage. It seems almost certain that the renal blood flow would be reduced greatly when marked hydronephrosis with thinning of the cortex takes place.

Three of the eight animals developed hypertension following obstruction of the ureters. Hartwich,[3] and Mason, Rainey, Resnik, Minot, Pilcher, and Harrison[4] similarly reported a rise in blood pressure in some animals following this procedure. Since hypertension occurs in some instances following partial obstruction of renal arteries,[5] and since the renal blood flow is diminished by ureteral obstruction, it seems that the same mechanism may be responsible for the rise in blood pressure following both of these experimental procedures.

The experiments of Hinman and his associates[6] would lead one to suspect that the renal blood flow is diminished in hydronephrosis. The arteries of the kidneys were injected with opaque material after varying degrees of hydronephrosis had been produced. They found that pelvic distention foreshortens and crinkles the interlobular and arteriolae rectae vessels and stretches and lengthens the interlobars and arcuates.

SUMMARY

The blood flow and oxygen consumption of the kidneys of unanesthetized dogs have been determined before and after the production of ureteral obstruction. The findings indicate that early hydronephrosis is associated with a decrease in the renal blood flow, little if any alteration in the arteriovenous oxygen difference, and a decrease in the oxygen consumption.

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THE CAUSE OF DEATH IN LIVER PERITONITIS

Blood Chemistry Findings in Dogs Subjected to Intraperitoneal Implantation of Fresh, Ground, Adult Dog Liver

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THE early experiments of Mason, Davidson, Matthew and Rastello[1] upon the toxic effect of intraperitoneal autolysis of dog liver, have stimulated numerous other investigations of the problem. Ellis and Dragstedt,[2] Andrews, Rewbridge and Hrdina,[3] and Dvorak[4] have shown that associated with autolysis of liver in vivo, there is an abundant growth of bacteria normally found in livers of adult dogs. At the present time there is considerable difference of opinion as to the pathogenic nature of these bacteria and the rôle they play in the early death of dogs following intraperitoneal injection of various preparations of liver tissue and bile salts. Ellis and Dragstedt[2] and Dvorak[4] concluded that bacterial peritonitis is the causative factor in the early death of the animals. Andrews, Rewbridge and Hrdina[3] stated that the organism is Welch's bacillus and that the rapid death of the animal is explained by this overwhelming toxemia. Furthermore, they were of the opinion that this organism lies dormant in the tissues of the dog and can be stimulated to produce a fatal infection by the intraperitoneal autolysis of *sterile* liver and bile salts.

We have found that the bacteria in adult dog liver usually consist of varying strains of both aerobic and anaerobic organisms. In every instance one of the organisms has been a large, anaerobic, sporulating bacillus which stains positive by Gram's method. In our studies[5] this bacterium produced no exotoxin, and was not identical with the Welch bacillus in either morphology or cultural characteristics. In a previous report,[6] we have shown that fresh liver sterilized by autoclaving does not cause death in dogs when injected intraperitoneally in 100 gram amounts. When, however, the liver is incubated for twenty-four hours or longer and is then sterilized by autoclaving, the intraperitoneal injection of 100 grams causes rapid death of the dog, though the peritoneum remains sterile.

Mason and his coworkers[1] concluded from their early investigations with fresh liver that the rapid death of the animals was due to absorption of toxic substances produced from intraperitoneal autolysis of the

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liver material. They pointed out the close correlation between their findings and those reported by Cannon in his investigations on traumatic shock. Later, Mason and Lemon[7] discussed anhydremia and loss of body fluids intraperitoneally as a contributing cause in the rapid death of the dogs. Recently, Mason and Nau[8] showed marked degenerative changes in the liver and kidney of dogs subjected to the intraperitoneal introduction of sublethal amounts of fresh liver tissue. They concluded that these changes were caused by the absorption of toxins liberated from autolyzing liver fragments.

In our studies we have made observations which we believe explain many conflicting interpretations of other workers. In all of our investigations, we have been impressed by the marked clinical picture of shock which is associated with the rapid death of dogs when certain preparations of liver are placed intraperitoneally. This report deals primarily with blood chemistry changes in dogs following intraperitoneal injection of *fresh* liver. In an attempt to ascertain whether the presence of bacteria in the peritoneal cavity was a contributing cause in the early death of the animals, smears and cultures were made of peritoneal exudate removed as the dogs were dying.

EXPERIMENTS UPON FRESH, GROUND, ADULT DOG LIVER

All investigators agree that when fresh, adult dog liver, ground or whole, is placed intraperitoneally in the experimental animal, the dog dies usually within twenty-four hours. Furthermore, it is a common belief that the amount of liver introduced has no bearing upon the time the animal survives. The amount of liver introduced has varied with different investigators from 30 to 100 grams.

In all of our experiments the liver was obtained from a sacrificed dog with aseptic surgical technic. As an added precaution against contamination, the liver was plunged into scalding water until the surfaces were coagulated. A small piece of the liver was removed and placed in a good anaerobic culture medium.[5] The remainder of the liver was ground in a sterile food chopper and placed in sterile Erlenmeyer flasks. The liver material plus an equal volume of sterile normal saline was placed intraperitoneally in the animals a few moments after it was removed from the sacrificed dog. The animals receiving the liver were given no food for twenty-four hours preceding the operation. They received a preanesthetic dose of morphine sulphate, ¼ gr., and atropine sulphate, $\frac{1}{150}$ gr. The operation was done under light ether anesthesia. The animals were then returned to individual cages and offered water. If they survived the operation twenty-four hours, they were offered food.

Experiment 1.—In this experiment an effort was made to ascertain whether the amount of fresh, ground liver placed intraperitoneally in-

fluenced the interval of time the animals survived. Varying amounts of liver were introduced into four dogs through small laparotomy incisions. Table I shows the results of the experiment.

In Table I, we give the data on four dogs only. The findings, however, are in agreement with general observations which we have made numerous times; namely, that fresh liver, even in small intraperitoneal doses, makes the animals acutely ill, but survival does occur. Dog 304, which received ½ gm. per kilo, a total dose of 5 grams of fresh liver, was prostrated for a number of hours, refused food, and for several days vomited blood. Smears and cultures made from peritoneal exudate removed eighteen hours postoperatively, were positive for the dog liver anaerobe. This dog, however, made a complete recovery in three weeks. We conclude, therefore, that the amount of liver introduced does have

TABLE I

THE EFFECT OF PLACING VARYING AMOUNTS OF FRESH, GROUND, ADULT DOG LIVER INTRAPERITONEALLY

	AMOUNT OF LIVER INTRODUCED THROUGH LAPAROTOMY INCISION		RESULT	SMEAR PERITONEAL EXUDATE 18 HR. POSTOPERATIVE	CULTURE PERITONEAL EXUDATE 18 HR. POSTOPERATIVE
	TOTAL GRAMS	GM. PER KILO			
Dog 304	5.0	½	Survived	Positive for dog liver anaerobe	Positive for dog liver anaerobe
Dog 301	17.5	1	Died 48-55 hours	Positive for dog liver anaerobe	Positive for dog liver anaerobe
Dog 302	37.5	3	Died 25-32 hours	Positive for dog liver anaerobe	Positive for dog liver anaerobe
Dog 303	67.5	5	Died 21-25 hours	Positive for dog liver anaerobe	Positive for dog liver anaerobe

a bearing upon the interval of time the animal survives. When, however, fresh, ground, adult dog liver is used in amounts of 30 grams or more, the animals all die rapidly, having the clinical appearance of shock associated with bacterial growth in the peritoneal cavity. When these larger amounts of liver are used, the calculated dose per kilo has little relationship to the time the animal survives.

Experiment 2.—This experiment was undertaken to determine the changes in blood chemistry which occurred following the intraperitoneal introduction of 100 grams of fresh, ground, adult dog liver. Six dogs were used. The following blood studies were done on the animals before placing the liver material intraperitoneally and later when the animals were moribund: red and white cell counts with the hemocytometer; hemoglobin estimation in the Haden-Hausser hemoglobinometer;[9] coagulation time by the venous puncture and test tube methods;[10] carbon dioxide capacity of the plasma by the Van Slyke volumetric method;[11] blood volume, plasma volume, and hematocrit number by the injection of vital red dye after the method of Hoople, Smith, Belt and Whipple;[12] blood sugar determinations, using the Folin and Wu macromethod

nonprotein nitrogen by nesslerization;[14] total nitrogen by the macro-Kjeldahl method;[15] blood chlorides as NaCl following the Volhard principle, using the Whitehorn procedure,[16] and the blood urea nitrogen by use of the Leiboff pressure tube.[17]

The liver material was obtained from sacrificed dogs, ground and placed intraperitoneally in the same manner as described in Experiment 1. All of the animals died from eleven to seventeen hours following the introduction of liver. Bacteriologic smears and cultures from peritoneal exudate, removed as the dogs were dying, showed the dog liver anaerobe to be present in each case. Since the findings in all 6 animals were similar, the results can best be shown by including a typical protocol and table. Table II shows physical and chemical changes in the blood observed when 100 grams of fresh, ground, adult dog liver are placed intraperitoneally.

PROTOCOL

2/3/36 DOG 294 TABLE II

A short-haired, male cur, well nourished and healthy. The animal had been starved for twenty-four hours and weighed 16.8 kilos.

4:15 P.M.—Samples of blood were taken for blood cell counts, coagulation time, and blood chemistry analysis.

9:00 P.M.—Given a preanesthetic of ¼ gr. morphine sulphate and 1/150 gr. atropine sulphate.

10:20 P.M.—Given a general ether anesthetic and prepared for aseptic surgery.

10:40 P.M.—Three-inch laparotomy incision made through the right rectus muscle.

10:45 P.M.—One hundred grams (6 grams per kilo) fresh, ground liver introduced intraperitoneally.

10:55 P.M.—Laparotomy incision closed and animal returned to kennels.

2/4/36

9:40 A.M.—Animal lying on side in coma. Breathing was slow and labored, and the pulse weak and thready. The dog was passing bloody mucus from the bowel.

9:45 A.M.—Samples of blood were removed for cell counts, coagulation time, and chemical analysis.

10:15 A.M.—Animal was dying. Ten c.c. of peritoneal exudate were removed by pushing a hot, 15-gauge, perforated needle through a cautery burn in the abdominal wall. Bacterial smears and cultures were made of the peritoneal exudate. Both smear and culture were positive for the dog liver anaerobe.

The animal lived eleven and a half hours after the liver material was introduced intraperitoneally.

In general, the blood changes observed in these animals were definite and consistent. Following the introduction of ground liver intraperitoneally, there was a concentration of red blood cells and hemoglobin. The total nonprotein nitrogen, total nitrogen as protein, and urea nitrogen were increased. The carbon dioxide capacity of the plasma, plasma volume, blood volume, blood sugar, blood chlorides, and coagulation time were decreased. The white cell count varied with different

animals; some showed an increase, others a decrease. In most instances the results obtained confirm the findings of Mason, et al.,[1] when chunks of fresh dog liver were allowed to autolyze in the peritoneal cavity of the dog. The one notable exception is that we find a marked decrease in the coagulation time. Our studies further show that there is a marked concentration of blood, as indicated by increased red cell count, increased percentage of hemoglobin, and decrease in plasma volume. The hematocrit determinations, however, would seem to show very little change in the animal reported in Table II. Our experience has taught us that hematocrit determinations are subject to considerable error.

The necropsy findings in these animals were characteristic and agree with the findings of others who have investigated the problem. The

TABLE II

PHYSICAL AND CHEMICAL CHANGES IN THE BLOOD BROUGHT ABOUT BY THE INTRAPERITONEAL INTRODUCTION OF 100 GRAMS OF FRESH, GROUND, ADULT DOG LIVER

DOG 294	NORMAL	AT DEATH 11½ HOURS
R.B.C.	7,370,000	10,230,000
W.B.C.	9,700	3,200
Coagulation time	2 min.	40 sec.
Hemoglobin—gm. per 100 c.c.	14	18
CO_2 Vol. %	60	56
Hematocrit—% cells	50	53
Per cent Plasma	50	47
Plasma Volume in c.c.	1,258	740
Blood Volume in c.c.	2,500	1,570
Blood Sugar—mg. per 100 c.c.	103	71
Total N.P.N.—mg. per 100 c.c.	18	57
Total N. (as protein)—gm. per 100 c.c.	26	30.1
Blood Chlorides as NaCl—mg. per 100 c.c.	502	465
Urea Nitrogen—mg. per 100 c.c.	9.7	22.8

peritoneal cavity contained from 200 to 300 c.c. of turbid brown fluid; masses of liver fragments were caught in the omentum; all the peritoneal surfaces were fiery red and congested. There was a serofibrinous exudate on all peritoneal surfaces. There was marked hemorrhagic enteritis, particularly in the mucosae of the gastric fundus, the duodenum, and ileum. The temperature of the peritoneal fluid was 105° to 107° F. No free gas was noticed when the animals were examined at the time of death. The lungs were pink with congestion, and bled freely from the cut surface. The results obtained indicated that the animals die with all the cardinal signs of shock, as proved by both clinical and laboratory findings. The various factors which may be responsible for the shock condition will be taken up later in the general discussion.

Mason and Nau[8] report that marginal portions of the liver lobes are less lethal than the same amount of liver material taken from the center of the lobes. They further state that marginal portions of the lobes are sterile while the central parts harbor bacteria. The authors used

from 30 to 35 grams of liver substance in their experiments. They concluded that the presence of bacteria in autolyzing liver probably contributes to the rapid death of the animal, but believe their action is largely that of bringing about a more rapid liberation of toxins from autolyzing liver fragments. Since our early investigations of the problem had shown the margins of adult dog liver consistently to contain bacteria, we decided to check Mason's observations.

Experiment 3.—The liver was removed from a sacrificed dog in the usual manner. A small piece of liver was removed from the margin of the lobe and a similar piece was removed from the central part. Both pieces of liver were shown by culture to harbor the dog liver anaerobe. The marginal portions of the liver lobes were trimmed away from the central portions and 100 grams of each fraction were placed intraperitoneally in two operated dogs through a laparotomy incision, in a manner described previously. Both animals died some fifteen hours later, at approximately the same time. It is probable that this lack of agreement with the findings of Mason and Nau is to be explained on the basis that we introduced larger amounts of liver. Our subsequent experiment bears out this concept.

Experiment 4.—It occurred to us that the rapid death of dogs subjected to intraperitoneal introduction of fresh, ground, dog liver might be due in part to factors related to the laparotomy wound. We, therefore, minced the liver material finely enough to be injected through a 15-gauge needle. This was accomplished by placing 120 grams of fresh, ground liver plus an equal volume of sterile normal saline in a 500 c.c. Erlenmeyer flask, together with a small handful of broken glass. The flask with its contents was placed in a mechanical shaker and violently shaken for fifty minutes. The preparation was then filtered through six thicknesses of gauze. This procedure results in the almost complete separation of cells and parenchymal tissues of the liver from blood vessels, bile ducts, and connective tissue. After straining the preparation, it was found that 70 grams of parenchymal liver tissue plus 120 c.c. of normal saline had passed through the gauze, while 50 grams of the original amount of liver remained behind as blood vessels, bile ducts, and connective tissue. The fragments of broken glass were removed from this fraction. Cultures taken of both fractions were positive for the dog liver anaerobe. The 50 grams of blood vessels, bile ducts, and connective tissue plus 120 c.c. of normal saline were placed intraperitoneally in a dog through a laparotomy incision. The fraction of liver containing the 70 grams of parenchymal tissue was injected intraperitoneally in a similar dog through a 15-gauge needle. In this experiment the animal which received the 50 grams of liver blood vessels, bile ducts, and connective tissue presented the usual clinical picture of shock and died twenty-five to thirty hours following the operation. Postmortem examination revealed intense peritoneal congestion and peri-

tonitis. On the other hand, the animal which received 70 grams of parenchymal elements of liver survived. At no time did the dog appear to be acutely ill. A sample of peritoneal exudate was removed twenty hours after the introduction of liver material. Stained smears made of this exudate were negative for vegetative forms of bacteria. A culture made of the exudate, however, was found positive for the dog liver anaerobe after three days' incubation. This was due probably to the presence of spores. The experiment was repeated with identical results. In this repeat experiment the animal which received the parenchymal elements was explored thirty-six hours following the implantation of liver material. There was some free fluid in the peritoneal cavity, and large masses of liver material were caught in the omentum. There was no violent congestion of peritoneal surfaces, such as is commonly seen when fresh whole liver is placed intraperitoneally. The incision was closed, and the animal made an uneventful recovery. Cultures and smears made of the peritoneal exudate at the time of this second operation were negative for any bacteria.

The results obtained in these preliminary experiments indicated that the parenchymal element of liver is much less toxic in its effects than the blood vessel, bile duct, and connective tissue elements. Furthermore, they indicated the surprising ability of the dog to sterilize large amounts of this contaminated material.

To check further the above observations and at the same time to ascertain whether the method of introducing the parenchymal elements of liver intraperitoneally influenced the results, the following additional experiment was carried out: The parenchymal element obtained from fresh livers removed from sacrificed animals in the usual manner was introduced intraperitoneally in 4 dogs. The dose of liver material equaled 6 grams per kg. In each of 2 dogs of this series, the parenchymal liver suspension was injected intraperitoneally through a needle. Each of the remaining 2 received the parenchymal liver suspension through a small laparotomy incision. All of these animals survived, and none appeared to be acutely ill. The dogs were given general ether anesthesia thirty hours after the introduction of the liver, and samples of peritoneal exudate were removed, using the cautery and needle technic. Smears made of these exudates showed large numbers of pus cells but no bacterial forms. Two of the cultures remained negative, while 2 were found positive after three days' incubation. The results obtained in this experiment confirmed those obtained in the preliminary experiments in every detail. They indicate that the manner of introducing the liver material intraperitoneally has no apparent effect upon the results. They further substantiate the previous observation that the cellular element of liver is decidedly less lethal in its effect than are the blood vessel, bile duct, and connective tissue elements. We believe that these results offer a satisfactory explanation of the observations re-

ported by Mason and Nau[8] that marginal parts of liver lobes are less lethal than central parts, since the periphery of the liver lobes contains a relatively larger proportion of parenchymal elements. We find that the dog liver anaerobe is present throughout all the liver substance. Since 70 grams of the parenchymal elements of liver were shown not to be lethal when introduced intraperitoneally in the experimental animal, it followed that a determination of physical and chemical changes in the blood brought about by the injection of such material would be of interest. Experiment 5 was therefore carried out.

Experiment 5.—Two 70-gram lots of the parenchymal elements of liver were prepared and injected into 2 dogs in the same manner as described in Experiment 4. Physical and chemical determinations were made upon samples of blood removed from these dogs before the liver material was placed intraperitoneally, and repeated twenty hours later. The results of the experiment are shown in Table III. Both of these animals survived the operation.

TABLE III

THE PHYSICAL AND CHEMICAL CHANGES IN THE BLOOD BROUGHT ABOUT BY THE INTRAPERITONEAL INTRODUCTION OF 70 GRAMS OF THE PARENCHYMAL ELEMENTS OF FRESH, GROUND, ADULT DOG LIVER

BLOOD STUDIES	DOG 273		DOG 274	
	NORMAL	AFTER 20 HR.	NORMAL	AFTER 20 HR.
R.B.C.	7,000,000	7,400,000	6,880,000	7,320,000
W.B.C.	12,950	15,200	17,700	14,200
Coagulation Time	3′ 30″	30″	2′ 40″	40″
Hemoglobin—gm. per 100 c.c.	13	13	13	13.5
CO_2 Vol. %	72	50	63	56
Hematocrit—% cells	49	46	49	48
Per cent Plasma	51	54	51	52
Plasma Volume in c.c.	1,330	1,294	1,010	1,050
Blood Volume in c.c.	2,600	2,390	1,980	2,020
Blood Sugar—mg. per 100 c.c.	87	98	100	93
Total N.P.N.—mg. per 100 c.c.	40	46	30	36
Total N. (as protein) gm.	14.2	21.3	13.8	21.4
Blood Chlorides—mg. per 100 c.c.	465	485	500	495

A comparison of Tables II and III shows that, in general, both physical and chemical changes in the blood are much less marked in animals subjected to the intraperitoneal introduction of 70 grams of parenchymal elements of the liver. For the most part any changes observed in Table III are almost within the limit of technical error. The increase in total nitrogen of the blood and the decrease in coagulation time and carbon dioxide capacity of the plasma were the same in each instance. These animals never showed any marked evidence of shock.

DISCUSSION

Our experiments show that when dogs are subjected to the intraperitoneal introduction of 30 or more grams of fresh, ground, adult dog liver, the animals die usually within twenty-four hours, with all the

cardinal signs of shock. Furthermore, physical and chemical changes in the blood closely correlate those reported by numerous investigators on the subject of experimental shock. We believe, therefore, that shock is the major factor contributing to the rapid death of the animals. The factors which initiate the shock condition are not determined. It is not the purpose of this report to discuss the different theories which have been advanced to explain the mechanism of traumatic or secondary shock. At the present time there is considerable confusion in the literature as to whether secondary shock is caused by the absorption of toxic substances which cause a relaxation and increased permeability of the venules and capillaries, or whether the entire shock syndrome is due to hemorrhage and loss of body fluids.

It has long been known that trauma to abdominal viscera is one of the most effective measures in establishing a condition of secondary shock in the experimental animal. It follows that the intraperitoneal injection of any chemical substance with irritating qualities might be expected to accomplish the same result. Andrews, Rewbridge and Hrdina[3] reported that 10 per cent solutions of bile salts placed intraperitoneally caused rapid death of the animal. Since they found large anaerobic bacilli in the peritoneal exudate, they attributed the rapid death of the animals to the pathogenic nature of these bacteria. We repeated their experiment, using more precaution against contamination of the peritoneal cavity, and observed that although the animals died the typical rapid death, the peritoneal cavity remained sterile. Postmortem examination revealed 300 to 400 c.c. of bright red fluid in the peritoneal cavity, with intense congestion of the viscera. Obviously, it is not necessary that bacteria play any rôle in the death of animals subjected to this type of chemical peritonitis. It is open to question whether the fatal shock condition of the animal was due to irritation of peritoneal surfaces, with loss of fluids intraperitoneally, or whether there was likewise the absorption of toxic substances which caused damage to parenchymatous organs and capillary dilatation and congestion elsewhere in the body. The intense enteritis, particularly in the ileum and duodenum, and the petechial hemorrhages on all visceral surfaces would indicate that there is actually an absorption of toxins. Mason and Nau[8] have reported that following the intraperitoneal implantation of sublethal amounts of fresh liver, there is marked toxic degeneration of the liver and kidney. We have made similar observations upon animals subjected to intraperitoneal implantations of various preparations of liver. We have noted furthermore that the adrenal glands show definite pathologic changes, amounting in some instances to actual necrosis of the gland. It is possible that part of the disturbance in water balance and the shock condition of the animal can be attributed to absorption of toxins, which cause acute degeneration and exhaustion of these parenchymatous organs. It is logical that the increase in total nonprotein

nitrogen and urea nitrogen, and the marked alteration of blood sugar occur as a result of acute damage to the liver, kidneys, and adrenal glands. Moon and Kennedy[18] published an excellent paper on the pathology of shock, in which they contrast the shock picture produced from gross hemorrhage with that produced by trauma to an extremity, or the intraperitoneal introduction of ground sterile muscle. In both latter instances there was marked capillary damage and dilatation, particularly in the lungs and gastrointestinal tract. These changes in the capillaries were not seen in the dog subjected to gross hemorrhage. The mere fact that shock can be caused by hemorrhage and loss of fluids alone, does not preclude the possibility that the absorption of toxic substances can likewise be the cause of secondary shock. Krogh[19] has demonstrated that capillary change and relaxation can be produced by a wide variety of chemical substances.

We found, however, that the intraperitoneal introduction of 70 grams of the parenchymal elements of fresh liver was essentially harmless to the animal. The dogs failed to present the marked picture of shock seen in animals subjected to an equivalent amount of fresh, ground, whole liver. On the other hand, 50 grams of the blood vessel, bile duct, and connective tissue fraction of liver caused the typical shock picture and death of the animal. We further observed that animals injected with the cellular elements of liver were able rapidly to sterilize the material, while animals receiving the other fraction died with bacterial growth in the peritoneal cavity. We do not know whether the presence of the dog liver anaerobe in the peritoneal cavity of these latter animals contributed to, or caused, the condition of shock. It is possible that their presence was coincidental and could be explained on the assumption that toxic substances from this particular fraction of liver blocked out the phagocytic defense powers of the peritoneum. It is also possible that the fresh, parenchymal elements of the liver were able to combine with any toxins present, and in this manner protect the animal against shock. Whatever the explanation, we have demonstrated that the toxicity of implanted liver material is associated with the blood vessel, bile duct, and connective tissue elements. We believe that this observation may have fundamental significance in determining the complexity of factors which operate in producing this particular type of experimental shock.

SUMMARY

1. Dogs, receiving intraperitoneal doses of 30 to 100 grams of fresh, ground, adult dog liver, die usually within twenty-four hours, showing all the signs and blood chemical changes of shock.

2. When the dose is less than 30 grams for an average dog, there is a definite relationship between the interval of survival and the amount of liver introduced. One dog receiving ½ gram per kg. (5 grams total dose) survived indefinitely.

3. In the dogs which died, peritoneal smears and cultures taken shortly before death consistently revealed growth of the dog liver anaerobe.

4. We have found the parenchymal elements of the liver to be relatively nontoxic. When these elements were separated from the blood vessel, bile duct, and connective tissue portions of fresh dog liver, 70 grams of the parenchymal tissue suspension caused neither death nor shock. However, 50 grams of the connective tissue suspension caused both shock and death.

5. Cultures taken of the parenchymal suspensions have consistently showed that this fraction of liver harbors the dog liver anaerobe. Nevertheless, smears and cultures of peritoneal exudate removed from dogs subjected to the intraperitoneal introduction of parenchymal suspensions of liver have shown that these animals rapidly sterilize the peritoneal cavity, even in the presence of large amounts of contaminated liver substance.

6. The dogs receiving the liver connective tissue suspensions rapidly died of shock and bacterial peritonitis, while the dogs receiving the parenchymal liver suspensions survived and remained well. This interesting observation merits further investigation.

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ACUTE APPENDICITIS

A Review of 518 Cases in the University of Minnesota Hospitals From 1932 to 1935

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APPENDICITIS causes the loss of 20,000 lives each year in the United States; the highest mortality rate of any of the civilized nations. The mortality of appendicitis in this country was 11.4 per 100,000 population in 1910; 13.4 in 1920; 15.2 in 1929; and 18.1 in 1930. The average age at death in 1930 was 32.4 years. The victims of appendicitis die at a more productive age than the victims of tuberculosis (36.8 years), of cancer (60.7 years), of nephritis (62.2 years), or of heart disease (64.7 years). A survey of published statistics reveals a great variation in mortality, depending upon the method of classification of cases, and the type of treatment.

There has been no appreciable decline in the mortality of appendicitis in the past twenty years. In 16,424 cases of acute appendicitis, Stanton reports a mortality of 5.4 per cent. Twenty years ago, he found that it was 6.2 per cent in 4,343 cases. The degree of professional dissatisfaction with such results is indicated by the fact that over eight hundred articles on appendicitis have been written in the past four years.

The reasons for the high mortality in acute appendicitis may be summarized as follows: (1) delay by the patient in seeking medical advice, (2) inadequate medical treatment, (3) use of purgatives, and (4) mistakes in diagnosis. An important factor which has not been sufficiently stressed is the fact that the therapy employed in late cases with extra-appendiceal extension is often too radical and contributes to the high mortality.

The operative mortality bears a definite relationship to the duration of the acute inflammatory process. According to Stanton, about 30 per cent of the patients operated upon during the first day and 40 per cent of those operated upon during the second day of the disease present noteworthy peritoneal exudate. By the third day from 60 to 80 per cent of the cases present peritoneal involvement. At the same time, the operative mortality jumps suddenly to about 10 per cent. This increase involves chiefly those cases with periappendiceal complications, that is, abscess and peritonitis.

There would be no problem of appendicitis if all cases were operated upon early, that is, within twenty-four hours, as the mortality then would be less than 1 per cent (our mortality is 0.3 per cent for the un-

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complicated cases). The real problem lies in the treatment employed when the disease has spread beyond the appendix. In many hospitals, it is routine practice to operate upon all cases of appendicitis when the diagnosis is made. The practice at the University Hospital has been more conservative, especially in dealing with late cases.

The treatment of appendicitis at the University Hospital, in brief, is as follows:

1. Every early case without clinical signs of periappendiceal extension is submitted to immediate operation.

2. Those which are apparently subsiding when first seen are allowed to subside completely before operation.

3. Conservative therapy, consisting of rest, hot packs to the abdomen, paraoral fluids, gastric siphonage, and sedatives, is carried out in most cases seen after the third day of the disease, and in all such cases with periappendiceal complications.

4. Transfusion and all other supportive measures are utilized in those patients with diffuse peritonitis.

5. Appendectomy, after conservative therapy, is deferred for from six to eight weeks to allow the inflammatory process to subside completely. Operation can be carried out more safely at the later date.

SURVEY

We present a series of 518 consecutive cases of appendicitis seen at the University of Minnesota Hospital from January 1, 1932, to January 1, 1935.

Of these 518 cases, 85 (16 per cent) were classified as "inactive." Two hundred fifty-eight (50 per cent) were acute but uncomplicated. One hundred seven (21 per cent) exhibited extraappendiceal localization (either abscess or local peritonitis). There were 68 with general peritonitis (13 per cent). There were thus 433 cases of acute appendicitis.

1. *Inactive Cases.*—This group consisted of 85 patients in whom the diagnosis was based upon the history alone. They were seen in a quiescent stage, the diagnosis having been made by the home physician who referred them to the hospital after the attack had subsided.*

Postoperative complications encountered in this group were 3 instances of wound infection, 2 of bronchopneumonia, 1 of upper respiratory infection, and 1 of atelectasis.

2. *Uncomplicated Acute Cases.*—There were 258 cases of uncomplicated acute suppurative appendicitis, of which 131 were females and 127 males. The average age of the group was twenty-one years.

One hundred sixty-three were operated upon immediately, without a death.

*Cases of acute appendicitis with complications, discharged from the hospital after conservative treatment and returning for operation, are listed under diagnosis made when they were first seen. For example, cases of generalized peritonitis treated conservatively, returning for operation, are listed as general peritonitis, etc.

In 95 cases operation was deferred, with one death. Operation in these 95 cases was deferred for the following reasons: (1) subsiding appendicitis, (2) duration of three days or more, and (3) acute upper respiratory infection, rheumatic fever, diabetes, and cardiac or renal disease.

Postoperative complications in these acute cases included 7 infected wounds, 5 instances of atelectasis, 3 of pelvic abscess, 2 of upper respiratory infection, and 1 each of bronchopneumonia, pleurisy, pyelitis, phlebitis, scarlet fever, pulmonary embolism, intestinal obstruction, and tapeworm. The single death in this group resulted from an infected hematoma and general peritonitis.

3. *Acute Appendicitis With Extraappendiceal Localization.*—In the third group, those with extraappendiceal extension (either local peritonitis or abscess) there were 107 cases (27 females and 80 males). The average age was thirty-one years.

Thirty-three were subjected to immediate operation, with two deaths.

Sixty-eight operations were deferred, with three deaths. Of these, 17 had abscesses drained and were advised to return for appendectomy, while 51 were discharged after conservative treatment and were advised to return six weeks later for appendectomy. Thirteen failed to return.

In the remaining 6 cases, no operation was advised because of advanced age, poor condition of the patient, etc.

The postoperative complications encountered in all cases with extraappendiceal localization were 13 wound infections, 5 cases of bronchopneumonia, and 3 upper respiratory infections. There were 2 instances of intestinal obstruction, 2 of fecal fistula, 2 of postoperative hernia, 1 of paralytic ileus, and 1 of parotitis. Complications encountered before operation included 2 cases of infection of the urinary tract, 1 of osteomyelitis of the spine, and 1 of diabetes mellitus.

4. *Acute Appendicitis With General Peritonitis.*—There were 68 cases (13 per cent of the total number) in this group, of which 24 were females and 44 were males. Thirty-eight were under fifteen years of age. The average age was thirty years.

In 8 of these patients appendectomy was performed immediately.

In 45, operation was deferred. Of these, 32 were treated conservatively and advised to return for appendectomy in six to eight weeks. In 13, abscesses were drained and the patients were advised to return for appendectomy. (Five failed to return.)

In 15 cases no operative procedure was done. These patients were all desperately ill on admission. There were 23 deaths in 68 cases of general peritonitis.

Complications encountered in this group included 20 instances of localized abscess, 5 of pneumonia, 3 of atelectasis, 2 of wound infection, 2 of intestinal obstruction, and 1 each of pylephlebitis with liver ab-

scesses, pyelitis, and postoperative hernia. Complicating factors encountered in this group were 4 cases of diabetes mellitus and 2 of hypertension.

Total Hospital Days.—The average hospital stay of those patients with uncomplicated acute appendicitis was 9.75 days; that of those with local complications (abscess, or localized peritonitis) 22 days; while those with general peritonitis averaged 23 days in the hospital. This includes the second stay of those readmitted for appendectomy.

Duration of Symptoms.—The duration of the symptoms prior to admission in the uncomplicated acute cases averaged 2.4 days. Sixty-six per cent of these patients were seen before 48 hours. The duration of symptoms in those with local complications was 6.1 days, 34 per cent being seen before 48 hours; while in those with generalized peritonitis, symptoms had been present for 3.5 days, 45 per cent being seen before 48 hours. Only 46 per cent of all cases were seen within 48 hours of the onset of symptoms.

Sixty per cent of the cases with simple acute appendicitis, 33 per cent of those with local peritonitis, and 70 per cent of those with general peritonitis gave a history of repeated attacks.

Cathartics.—Cathartics were taken by 6.5 per cent of the patients with simple acute appendicitis, by 29.0 per cent of those with localized findings, and by 28.0 per cent of those with general peritonitis. Forty-seven per cent of those who died had taken cathartics. Complete information was not available in all cases.

Bowers, analyzing the mortality record of twenty-eight Philadelphia hospitals, showed that of those taking no cathartic during the acute attack, 1 in 80 died; of those taking a cathartic once, 1 in 13 died; and of those who were purged more than once, 1 in 7 died. In a recent analysis Hobler found that repeated catharsis was associated with a mortality of 20 per cent. Since repeated catharsis usually means a late case, it is difficult to evaluate the exact influence of catharsis alone upon the mortality. There can be no doubt, however, that the increased peristalsis and resultant increased intraappendiceal pressure which obtains may cause perforation of a tense gangrenous appendix and lead to dissemination of the infection.

Physical Findings.—Pain and tenderness were the only constant findings, being present in all cases. The average temperatures were 99.2° F. for uncomplicated cases and 101.5° F. for those with extraappendiceal extension. The leucocyte count varied from 12,300 in the uncomplicated cases to 19,000 in the diffuse peritonitis group. The presence of a rapid pulse, a temperature over 101°, and an increased leucocyte count are the result of the systemic reaction following peritoneal contamination.

Chills were present in 3.8 per cent of cases of simple acute appendicitis, 11 per cent of the complicated cases with abscess, and 6 per cent

of the cases with general peritonitis. Diarrhea was an infrequent symptom, being present in 7.7 per cent of the simple cases. Of the complicated cases, 20 to 25 per cent had diarrhea, of which one-fourth had taken cathartics.

Suppurative Complications.—Death in appendicitis is almost always due to intraperitoneal suppuration. Suppuration may localize in any quadrant of the abdomen, in the culdesac and in the subphrenic area. Suppurative pylephlebitis in this series was a rare complication.

Of 107 cases of localized suppuration 33 cases were submitted to immediate operation because of the failure to ascertain clinically that the process had spread beyond the appendix.

In 55 cases, because it was evident that an extraappendiceal complication was present, conservative therapy was instituted upon admission to the hospital. In only 17 of these did the inflammatory mass fail to resolve, necessitating surgical drainage of the abscess.

Forty-five cases of generalized peritonitis were treated conservatively. Twenty cases developed localized inflammatory masses; 13 of these necessitated incision and drainage in hospital. Seven subsided without surgical intervention.

Time of Operation.—Immediate operation was carried out in 47 per cent of all the acute cases. In 45 per cent, operation was deferred to a later date. Eight per cent of the cases were not operated upon.

Total Complications.—There were 22, or 3.8 per cent, wound infections; 25, or 4.8 per cent, respiratory complications. Five (1 per cent) of the cases developed intestinal obstruction.

ANALYSIS OF DEATHS FROM APPENDICITIS: JANUARY, 1932, TO JANUARY, 1935

There were 37 deaths in the whole group. Eight of these have been omitted from the study for the following reasons: one died from the anesthetic; 1 had severe Addison's disease and developed appendicitis while moribund from that condition; 1 was not seen by the surgical staff; 2 had appendectomy elsewhere and were admitted in extremis with diffuse peritonitis; the remaining 3 were moribund on admission, and died within 24 hours. This leaves 29 cases to be analyzed.

Sixteen of these were males and 13 were females. Nineteen were adults and 10 were children (15 years or under). The average age of the adults was 42 years. The average age of the children was 10 years, the youngest being 2 years. The average age of the entire series was 31 years. Thirty-five per cent of the patients gave a history of recurrent attacks. The duration of the symptoms prior to admission to the hospital averaged about 75 hours. Fifty-six per cent were seen 48 hours or more after the onset of the disease.

Pain was present in all cases, nausea in 96 per cent, vomiting in 86 per cent, anorexia in 90 per cent, chills in 13 per cent, and diarrhea in 17 per cent (13 per cent with catharsis, 4 per cent without). A history of catharsis was obtained in 47 per cent (14 cases). The cathartic was prescribed by a physician in 3 of these instances.

Tenderness to abdominal and rectal palpation was present in all, rigidity in 97 per cent, rebound tenderness in 83 per cent, abdominal mass in 17 per cent, and a mass on rectal examination in 20 per cent.

The temperature on admission averaged 101.2° F. The average pulse was 112, and the average leucocyte count 19,100. Polymorphonuclears averaged 84 per cent. Total stay in the hospital averaged about 8 days. Eight patients lived less than three days after admission. Twenty of the entire group had diffuse peritonitis on admission. Eight had appendicitis with local complications (6 abscesses, 2 local peritonitis). One had simple acute appendicitis which was allowed to subside before operation, but died of complications incident to operation.

Seven of the cases were treated by immediate operation, and in an equal number operation was deferred. Fifteen were not operated upon. In the cases in which operation was deferred, incision and drainage of a pelvic abscess through the rectum was done in 3 cases, and colpotomy was performed in one. Two patients were operated upon because the question of strangulation obstruction arose. Both proved to have general peritonitis and died following operation.

Cause of Death.—Twenty-three of the 29 patients who died were subjected to necropsy. Four more had been operated upon, so that the diagnosis was definitely established in 93 per cent. General peritonitis was the cause of death in 24 cases. There were 6 cases of abscesses in the culdesac, 4 of pneumonia, 3 of atelectasis, 3 of diabetes mellitus, 3 of multiple abscess formation, and 3 of intestinal obstruction. There were 2 cases of pleural effusion, and 1 each of acute upper respiratory infection, of pylephlebitis with abscesses in the liver and gallbladder, of parotitis, of impetigo, of toxic nephritis, of local peritonitis, and of paralytic ileus. The cause of death was usually a combination of factors with the toxemia of general peritonitis a common denominator.

TABLE I

MORTALITY STATISTICS OF UNIVERSITY OF MINNESOTA HOSPITAL CASES FROM JANUARY 1, 1920, TO JANUARY 15, 1929. (TASCHE AND SPANO.) ALL TREATED BY IMMEDIATE OPERATION

	CASES	DEATHS	MORTALITY PER CENT
Inactive	339	1	0.3
Acute suppurative	72	1	1.4
Acute suppurative with local peritonitis	156	4	2.5
with abscess	112	11	9.7
with diffuse peritonitis	21	8	38.0
Total	700	25	3.4

TABLE II

UNIVERSITY OF MINNESOTA HOSPITAL CASES FROM JANUARY 1, 1932, TO JANUARY 1, 1935. (SPERLING AND MYRICK.)

	CASES		DEATHS	MORTALITY PER CENT
Inactive	85	343	0	0
Uncomplicated acute suppurative	258		1	0.30
Acute appendicitis with abscess formation	75	175	3	4.0
Acute appendicitis with local peritonitis	32		2	3.2
Acute appendicitis with general peritonitis	68		23	33.8
Total	518		29	5.6
All uncomplicated cases	343		1	0.29
All cases with complications	175		28	16.0
	518		29	5.6

COMMENT

Prior to 1929, every case of appendicitis admitted to the University Hospital was treated by immediate operation, regardless of the stage of the disease, unless the patient was moribund. Statistics from 1920 to 1929 have been summarized by Tasche and Spano. It is apparent that there has been some improvement; that is, a decrease in mortality in that group of cases which presented some localization of the process at the time of admission (abscess or some local peritonitis). Our mortality in this group with abscess formation is 4 per cent. Reid, in a large series of cases treated by immediate operation, recently reported a mortality rate of 11.45 per cent. While it is obviously difficult to compare mortality rates in different series, such a difference would seem to be significant.

While there has been no great reduction in mortality rate in the group of cases with general peritonitis, it is noteworthy that the incidence of general peritonitis from 1932 to 1935 is four times that of 1920 to 1929; that is, 13 per cent as compared to 3 per cent. The mortality rate in this group of cases with general peritonitis, 33 per cent treated conservatively, compares favorably with that of other series in which all cases were submitted to immediate operation. (Reid.) Although from a comparison of mortality rates alone it would seem that some of these patients will die regardless of the type of treatment instituted, it is our clinical impression that these patients with general diffuse peritonitis, many of whom were desperately ill when first seen, having been transported one hundred to two hundred miles to the hospital, do better under the conservative treatment already described.

The question of when to operate is a difficult one, when patients are admitted late in the course of the disease. If it is plain that the process has already spread beyond the walls of the appendix, immediate operation is not recommended, although it is admittedly often difficult to determine whether perforation has occurred. A long history coupled with a moderately severe systemic reaction (fever of 101° F. or more,

elevated pulse rate, and marked physical findings) usually point to peritoneal complications. In such cases conservative therapy is indicated.

Patients admitted with a mass in the right lower quadrant are likewise best treated conservatively when first seen. Many of these masses will disappear spontaneously without surgery, and the patient can return six to eight weeks later for operation when all the inflammatory reaction has resolved. If, however, fever persists, and a tender mass is encountered, it is apparent that an abscess is present, necessitating evacuation and surgical drainage. This is ordinarily best done through a lateral oblique incision which is an extraperitoneal approach. Collections of pus in the culdesac may be drained by colpotomy or incision through the rectum. Drainage per rectum carries with it a definite danger, as shown by the fact that two deaths followed this procedure. The introduction of bacteria from the rectum into the abscess cavity, establishing there a new bacterial flora, may have influenced the outcome. Incision and drainage of a pelvic abscess by rectum should be delayed until the mass is of good size and fluctuation can be demonstrated. Colpotomy in the female may be done without hazard. There were no deaths following this procedure.

It is very important to differentiate between an inflammatory mass about the ruptured appendix, which may gradually resolve, and a true appendiceal abscess with gross pus formation. The infiltration type of mass should be left alone; i.e., treated conservatively. The true abscess should be drained through some extraperitoneal approach.

Many of the localized masses, which were palpated on admission, disappeared under conservative treatment. Many of these when first seen no doubt represented loops of bowel matted together by omentum and fibrinous peritoneal exudate, and resolved without gross suppuration. In these cases, if fever persists and the mass does not recede in size, an accumulation of pus is usually present and should be evacuated. Further delay then is dangerous, as it invites rupture of the abscess into the general peritoneal cavity. Such a catastrophe is usually accompanied by a severe degree of shock, from which the patient fails to rally in spite of transfusions and other supportive means. Lethal exitus ensues very rapidly.

Suppurative pylephlebitis may possibly have its origin in undrained collections of pus in the peritoneal cavity. This complication, however, was observed only twice in our entire series of cases.

Subphrenic infection follows perforated suppurative appendicitis not infrequently, but in our experience it usually subsides without the formation of an abscess requiring surgical drainage. In this series it was necessary to drain only one such subphrenic abscess.

In many of the cases of diffuse peritonitis which were treated conservatively, films were made with the patient in an upright position.

This was done in order to search for gas under the diaphragm and thus rule out the presence of a perforating lesion of the gastrointestinal tract. These studies were all negative, including those in which perforation of the appendix had occurred; a walling-off process apparently effectually prevents any upward displacement of gas which may escape at the time of perforation. When the appendix ruptures, communication of the intestinal canal with the peritoneal cavity does not obtain in the same manner as when a break exists in the stomach or colon.

One should refrain from any attempt to remove the appendix when draining an abscess in the right lower quadrant, if the appendix is embedded in the adhesions forming the wall of the abscess. By too vigorous manipulation, this protective wall may be broken and the infection spread throughout the peritoneal cavity, with disastrous results.

Drainage.—Indiscriminate drainage of the peritoneal cavity is an error that contributes to postoperative complications, such as hernia, fecal fistula, adhesions, and intestinal obstruction. It results in a longer hospital stay and increases the mortality. It has been shown that draining the peritoneal cavity after an appendectomy, when only a cloudy protective fluid is found at operation, inhibits the defense reaction of the peritoneum. In such cases the patient makes a better recovery when the abdomen is closed tightly. Drainage without adequate indication is better omitted.

Incision.—The McBurney incision is employed at the University of Minnesota Hospital. When correctly made, it affords adequate exposure and may easily be lengthened in either direction. It approaches the peritoneal cavity from its lateral aspect, and should pus be unexpectedly encountered, it is drained through the lateral gutter instead of into the general peritoneal cavity. Shute recently reported the mortality for the right rectus incision as being 33.3 per cent in the diffuse peritonitis group, 30 per cent in the group with local peritonitis, and 33.3 per cent in those with early abscess formations; while for the McBurney incision he reported the mortality to be 16, 6, and 6.6 per cent respectively. Reid recently reported a decrease in mortality from 9.5 to 5.4 per cent since the routine use of the McBurney incision was adopted. It has been proved by experience that long incisions, allowing good exposure and free approach, are much safer than small incisions, which may necessitate too much traction during the most delicate part of the operation, that of freeing the diseased appendix. The edematous, gangrenous appendix may easily rupture during attempts to deliver it blindly through a "buttonhole" incision.

CONCLUSIONS

1. The mortality from acute appendicitis is still too high.

2. The probable reasons for this high mortality are (a) delay, (b) catharsis, (c) meddlesome surgery after the infection has spread beyond the appendix.

3. Every case of appendicitis in which the process is confined to the walls of the appendix should be operated upon immediately. Those with extraappendiceal complications, such as abscess or diffuse peritonitis, are best treated conservatively.

4. Operation after the first 48 hours of the disease should be done only in selected cases.

5. The operative mortality is highest from the third to the sixth day, as the operation is done while nature is still trying to localize the infection.

6. If an abscess is encountered at operation, too strenuous efforts to remove the appendix should be avoided, especially if it is buried in adhesions.

7. Buttonhole incisions are best avoided. That of McBurney is recommended.

8. Indiscriminate drainage of the peritoneal cavity predisposes to postoperative complications and should be avoided.

9. Drainage of culdesac abscesses per rectum carries a definite hazard and mortality. Colpotomy in the female is a relatively safe procedure.

10. Five hundred and eighteen consecutive cases of appendicitis are reviewed. An analysis of the 29 deaths in this group during the three-year period (1932-1935) is presented.

11. The mortality statistics of the group treated conservatively are sufficiently good to merit a continuation of this type of treatment in the hope that we will learn to use it more intelligently as time goes on.

12. The treatment of diffuse peritonitis is still unsatisfactory, and the mortality is still high (33 per cent).

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EVIPAL ANESTHESIA: A CLINICAL STUDY OF THREE HUNDRED CASES

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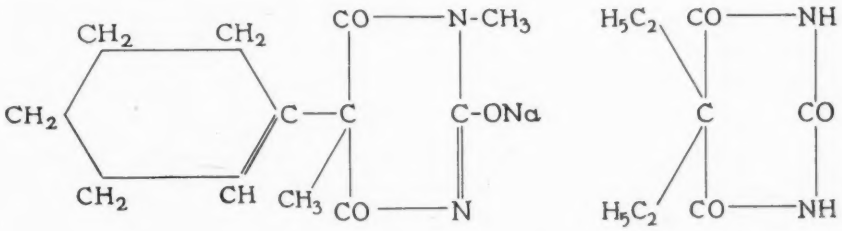
THE introduction of sodium evipal to clinical use has provided the surgeon with an anesthetic which is remarkable for its ease of administration, rapidity of induction, and freedom from unpleasant sequelae. Originally introduced as "the ideal anesthetic for short surgical procedures," this new drug is possessed, on the one hand, of certain properties which make its indiscriminate administration dangerous, and on the other hand, of unique qualities which render desirable a widening of its scope to include more than "short surgical procedures." In the following paper, certain characteristics of the drug with which we have been impressed during a two-year clinical study are reported.

Evipal, or evipan, was introduced as an intravenous anesthetic by Weese and Scharpff[1] in 1932. It is a white, water-soluble powder, now supplied in one gram sterile ampules to be dissolved in water at the time of use to make a 10 per cent solution. Chemically, it is related to barbital, as it is made by the methylation of the mild hypnotic phanodorn. The similarity of these compounds may be seen from the accompanying formulas (Fig. 1).



Evipal Barbital

Fig. 1.

Most of the investigations upon which the clinical use of evipal has been based were conducted by Weese[1, 2] in the laboratories of the I. G. Farbenindustrie, the German manufacturers of the drug. Weese reported that evipal had a wide margin of safety, as laboratory animals tolerated about three to four times the minimal active dose. When lethal doses were given, the respiratory center was affected before the heart, and if the anesthesia was not too deep, the animals could be

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revived by artificial respiration. In contrast to the previously known barbiturates, evipal was remarkably free from manifestations of increased excitability and was very quickly destroyed by the body. In the rabbit, one-half of the maximal narcotic dose was broken down in thirteen minutes. Weese considered the liver to be the principal detoxifying organ, because hepatectomized animals awoke more slowly from the effects of the drug than normal or nephrectomized animals. Maloney and Hertz[3] have confirmed the observations of Weese in regard to the coefficient of effectiveness of evipal. They found the toxic-anesthetic-hypnotic ratio in rats to be 100:36:18. Observations on a small number of dogs have convinced us that freedom from excitability is not invariable; that morphine seems to deepen and prolong the anesthesia; and that there is a great individual variation in the effective dose, as Weiss[4] has emphasized as a characteristic of the barbiturates.

CLINICAL OBSERVATION

During the last two years, over 300 operations have been performed under intravenous evipal at the Peter Bent Brigham and Beverly Hospitals. As can be seen from Table I, this included a wide variety of operative procedures. No attempt has been made to limit the use of evipal to the so-called "good-risk" patient, but in selected instances, we have used the drug whenever its singular qualities were particularly indicated. Comparatively few patients suffered, however, from conditions of serious magnitude other than the surgical condition requiring operation. A few were cardiac patients; one had intractable angina; six suffered from moderately severe diabetes; two had advanced tuberculosis; and three had chronic glomerular nephritis. In none of these cases were untoward reactions observed, but in all but one of these patients, the operative procedures were of a minor nature, and the amount of evipal used was less than 10 c.c.

In general, our observations are in accord with those of other investigators. The intravenous injection of sodium evipal usually induces the rapid onset of quiet anesthesia which is not unlike natural sleep. Respirations are slowed and slightly deepened. The pulse if previously rapid from excitement tends to slow, and frequently there is a fall in blood pressure. Tonic or clonic contractions of muscles, more or less generalized, may occur during the stage of induction. These seem to be particularly induced by painful stimuli, and many persist throughout the operation if full relaxation is not obtained. In favorable cases, with the use of preoperative medication, deep anesthesia sufficient to dilate the rectum or open the abdomen can be obtained. By the fractional administration of the drug, a method which we believe should invariably be employed, full anesthesia can be maintained for an hour or longer.

TABLE I

General Surgery	
Appendectomy	1*
Laparotomy	4
Colostomy	2
Herniorrhaphy	1*
Resutured abdominal wound	2
Débridement of burns	2
Minor amputation	4
Minor fracture	19
Excision of carbuncle	12
Biopsy	2
Incision and drainage	75
Miscellaneous	15
Hemorrhoidectomy	2
Fistula in ano	1
Proctoscopy	2
	144
Urology	
Total cystectomy	1*
Cystectomy	2*
Suprapubic prostatectomy	3*
Transurethral prostatectomy	6
Ureteral transplantation	1*
Excision hydrocele	2
Circumcision	6
Dilatation of urethra	6
Cystoscopy	18
Incision and drainage of epididymis	1
Insertion of radium into prostate	1
	47
Thoracic Surgery	
Bronchoscopy	2
Esophagoscopy	3
Rib resection	6
	11
Gynecology	
Dilatation and curettage	6
Dilatation and curettage; biopsy of cervix	2
Pelvic laparotomy with drainage of pelvic abscess	2
Posterior colpotomy	3
Cauterization of cervix	1
	14
Ear, Nose, Throat	
Drainage of antrum	10
Tonsillectomy	2
Incision and drainage of peritonsillar abscess	1
Paracentesis of ear	1
Excision of nasal polyp	1
	15
Dental	
Extraction of teeth	59
Excision of root tip	5
Incision and drainage of alveolar abscess	6
Reduction and wiring of fractured jaw	5
	75
Total	306

*Evipal used to supplement spinal or local.

Most observers consider rapidity of recovery to be one of the advantages of evipal anesthesia, but we have found that the recovery rate varies considerably with the duration of the anesthesia. In simple cases, where only 3 to 5 c.c. of the drug are used, recovery is usually immediate and is remarkably free from unpleasant after-effects. Occasionally, however, even with small doses, recovery may be prolonged. Thus, in one case for no apparent reason, the recovery rate was prolonged to ninety minutes following the administration of only 5 c.c. of evipal. When large doses are used, the recovery period is greatly prolonged. We have had patients remain unresponsive for several hours following the administration of intravenous evipal in amounts varying between 12 and 20 c.c. Although the recovery period even in these cases is usually free from unpleasant sequelae, from the point of view of the rapidity of the recovery alone, evipal has proved inferior to nitrous oxide for operations of long duration. In our experience, the use of carbon dioxide inhalations and coramine injections has not shortened the recovery period, but it is only fair to say that we have used coramine in small doses only.

Certain features of evipal anesthesia require particular emphasis. First, evipal possesses the disadvantage common to all intravenous drugs, that once administered, its action is irrevocable. This fact alone renders the fractional method of administration imperative. Moreover, this inherent danger of the intravenous route is increased by a great individual variation in the effective dose. Thus, in one instance a young boy weighing only 134 pounds required 20 c.c. of evipal before sufficient relaxation was obtained to incise and drain an abscess of the leg, a procedure lasting only six minutes, while in another case, 6 c.c. permitted the total excision with endothermy of a large carbuncle of the neck in a woman weighing 229 pounds. The latter procedure lasted ten minutes. *It is obvious, therefore, that no rule can be established in regard to dosage and, as described below, the fractional method of administration should invariably be used.*

It follows as a corollary of this variation in the effective dose that certain patients are highly resistant to evipal anesthesia. In 5 per cent of our cases, 10 c.c. or more of evipal have failed to produce sufficient relaxation, even with preoperative medication with morphine; and in another 10 per cent, the relaxation, although sufficient to permit operation, has not been satisfactory. This constitutes one of the chief disadvantages of the drug, because as yet there is no way of predicting which patient will prove resistant. Two of our patients who were particularly difficult to anesthetize with evipal were negroes.

It is our impression that the preoperative use of morphine is of definite value in obtaining more satisfactory relaxation. This was very strikingly exemplified in the case of a young negro to whom evipal

was given on five different occasions for the dilatation of an urethral stricture. Without preliminary medication 10 c.c. were required for the passage of only one or two sounds. After medication with 15 mg. of morphine and 100 mg. of luminal, satisfactory relaxation was obtained for several minutes with only 6 c.c. of evipal. The recovery period was not prolonged by the use of the preliminary medication.

The third characteristic of evipal anesthesia with which we have been impressed is the tendency of the drug to cause a fall in blood pressure. According to Jarman and Abel,[5, 6, 7] who have had a very extensive experience with evipal and whose excellent contributions should be read by all who use the drug, evipal uniformly causes a fall in blood pressure. This has not been our experience, possibly because we have taken pressure readings at five-minute intervals and may have overlooked a brief transitory fall in pressure occurring during the first few minutes of anesthesia. However, in 100 cases in which we have recorded the blood pressure at five-minute intervals, a significant variation, 20 mm. of mercury or over, has occurred in forty. In twenty-nine of these, there was a considerable fall; in three, a definite rise; in six, a fall followed by a rise; and in two, a rise followed by a fall. A fall in blood pressure when it occurs may be very marked, however, and as Jarman and Abel have emphasized, a patient whose blood pressure is already abnormally low should not be given evipal. The fall in blood pressure has been so striking in some of our cases that we feel that the prolonged use of evipal in major cases might predispose to shock. The exact mechanism of the fall in blood pressure has not been determined.

Fourth, the effect of evipal on the respirations is of considerable importance. The drug is a definite respiratory depressant. This has been emphasized by all observers and unquestionably constitutes a real danger. In 15 per cent of our cases, slight cyanosis has persisted throughout the operation although an adequate airway was maintained, and in two cases transitory cessation of respiration occurred. In both of these latter cases too rapid administration of the drug was made. Fortunately respirations were resumed almost immediately without the necessity of supportive measures. In addition to a depression of the respiratory center under evipal anesthesia, temporary obstruction to the air passage may occur from falling back of the tongue and relaxation of the jaw. This fact indicates the need of an anesthetist in addition to the one administering the drug. Finally, in certain cases evipal may induce severe asthma. We have had two such cases, and Feldweg[8] strongly cautions against the use of evipal in asthmatics. In both of our cases, the attacks came on almost immediately after the injections were started. They were characterized by marked cyanosis, stridor, and irregular labored breathing. In both

cases the attacks subsided as soon as full anesthesia was obtained, but recurred in an equally alarming manner during the recovery period. For the present, we consider a history of asthma to be a contraindication to evipal.

Rapidity of recovery and freedom from unpleasant sequelae are considered to be two of the great advantages of evipal anesthesia. Except as we have already emphasized, that recovery may be greatly prolonged if large doses are used, our experience confirms this impression. Nausea and vomiting are rare, occurring in 2 per cent of our series. Headache is not common; it occurred in 6 per cent of our patients. Postoperative excitement is occasionally encountered, particularly in alcoholics. Although usually transient, it rendered one of our patients quite unmanageable for several minutes after regaining consciousness. Pulmonary atelectasis occurred in 3 per cent. As most of our patients suffered from comparatively minor surgical conditions, it is fair to say that in major surgery the incidence of pulmonary atelectasis would not be lower after evipal than after another general anesthetic.

A postoperative complication of considerable importance is a state of amnesia. Five of our patients suffered from this condition for periods of thirty minutes to twelve hours after apparent complete recovery. We consider this a contraindication to the use of evipal on out-patients, unless they are to be hospitalized or special arrangements are made to care for them during their return home. Other examples of damage to the nervous system following evipal anesthesia are the case of complete paralysis of the trunk, lower limb, and distal portions of the upper limbs reported by Landor and Salleh;[9] the case of markedly increased intracranial pressure reported by Landau and Wooley;[10] and the case of polyneuritis reported by Palmer.[11] It is difficult to evaluate these complications. We have had no similar difficulties, and none have been observed in the very large series of Jarman and Abel.[6]

FATALITIES

Reported fatalities due to evipal anesthesia have been rare. Stimpfl[12] in an analysis of eleven deaths found in most cases a relative overdosage. It is worth noting, however, that all of his cases received less than 10 c.c. of evipal, and in one instance only 4½ c.c. This again serves to emphasize the importance of individualization in the use of sodium evipal intravenously. Attention must be directed, not so much to the total amount, as to the time in which any given amount is administered. In Stimpfl's cases, the manner of death appeared to be equally divided between respiratory and cardiac failure.

In our own experience there have been no fatalities attributable to evipal anesthesia, although three patients who have had evipal have died; one, two days after operation, and the others, ten days after

operation. In all three cases, recovery from the anesthesia was complete, the patient dying of the condition for which the operation was undertaken. One of these cases, that of a man forty-five years of age who was suffering from extensive actinomycosis of the lungs, pleura, liver, and brain, is of particular interest. This patient received evipal on six different occasions, five of them within a period of five weeks before death. The total amount given was 30.5 c.c. Careful postmortem studies of the brain, liver, and kidneys have shown no changes which could be attributed to evipal.

TECHNIC

After a study of our first one hundred evipal anesthesias, the following technic was adopted, and is being used at present with minor variations at the Peter Bent Brigham and Beverly Hospitals:

(a) *Preoperative Preparation.*—Breakfast is withheld from patients routinely. On several occasions we have given evipal to patients within an hour after a heavy meal without ill effects, but this should be avoided if possible, as untoward reactions have been reported.[13] For procedures of short duration, such as the incision and drainage of a small abscess, no preliminary medication is given. For a longer operation such as cystoscopy, transurethral resection, rib resection, or abdominal section, preliminary medication with morphine in doses of 10 to 15 mm. is given one hour before operation. It has been argued[14] that to add the depressant action of morphine to that of evipal increases the danger of respiratory paralysis. We are entirely in sympathy with this view, but feel that if the fractional method of administration is used, there is not sufficient danger of respiratory paralysis to contraindicate premedication with morphine. Without premedication the scope of evipal anesthesia is greatly limited, and increased dosage must be given.

(b) *Administration.*—The operative field is completely prepared before starting the injection. A suitable vein in the antecubital fossa is selected, and the arm extended in a comfortable position on an arm board. In our earlier experience, we insisted upon having an anesthetist present in addition to the one giving the anesthesia to keep an accurate record of pulse, respirations, and blood pressure, and to hold the jaw, insert an airway, or administer oxygen if necessary. At present, in minor cases, a record of pulse, respirations, and blood pressure is occasionally omitted. The drug is dissolved in sterile water several minutes before the final preparations of the patient are completed. Having the drug in solution for several minutes before the injection seems to help minimize tremors. Injection is made with a 10 c.c. Luer Lock Syringe, using a good sized needle (No. 19), because if the operation is prolonged, there is less danger of clotting.

(c) *Dosage.*—As has already been emphasized, no rules regarding dosage can be established. To individualize correctly is the art of evipal narcosis. Depending upon the weight, degree of excitement, amount of preoperative medication and general condition of the patient, we inject from 2 to 4 c.c. very rapidly (that is, 1 c.c. every ten seconds), and then wait thirty seconds to observe the result. This short pause following the initial injection is very important because as Killian[15] has emphasized, although the curve of effectiveness of evipal rises very quickly, the maximum effect is always reached after several minutes, so that it is possible to exceed the minimal fatal dose during the first few seconds of administration. This is particularly important if preoperative medication is used.

In the vast majority of cases, following the initial injection, the patient, who has been instructed to count, suddenly stops counting, takes a long sigh, and passes into a fairly deep anesthesia. Then one more cubic centimeter is injected, and the operation started. As needed, more evipal is injected in amounts of one-half to one and one-half cubic centimeters. If tremor is marked or there is extreme rigidity, more evipal is needed. Apart from obvious signs of awakening such as moving or moaning, the most helpful indications of the depth of anesthesia have been the rigidity of the jaw and the size of the pupils. If anesthesia is deep, the pupils are large and fixed, while with regaining consciousness the pupils become smaller and react to light.

The question naturally arises as to how much evipal can be given at one time. Provided the condition of the patient is satisfactory, we have continued with the fractional administration of the drug until the operation was completed. In ten instances we have used between 12 and 20 c.c. of the drug and have observed no untoward effects. It may be said, however, in regard to large doses, that there seems to be a progressively greater depressant effect of the drug when larger doses are used, with the result that recovery is frequently greatly prolonged. Although amounts of evipal as great as 30 to 40 c.c. have been administered[16] without apparent unfavorable result, our experience would lead us to be very cautious in using over 15 c.c.

(d) *Postoperative Management.*—Following the operation, the pulse, respirations, and blood pressure were taken at ten-minute intervals until full consciousness was regained. In minor cases this is no longer deemed necessary. Once consciousness has been regained, patients may be permitted to eat if they so desire. We have insisted upon patients' remaining in the hospital overnight following evipal anesthesia. This was originally done as a precaution in the use of a new drug and to provide an opportunity for a careful observation of the recovery period. Because of the occasional occurrence of amnesia, however, we still hospitalize out-patients following evipal narcosis, making exceptions to this rule only in particular instances.

CONTRAINDICATIONS

Jarman and Abel[7] consider liver damage, low blood pressure, the sitting position, and previous medication with barbiturates as definite contraindications to evipal. As the available evidence points to the liver as the principal detoxifying organ for evipal, it seems reasonable to consider jaundice, cirrhosis, or other evidences of liver damage as a definite contraindication. In our opinion, low blood pressure, the presence or imminence of shock, and marked debilitation also constitute definite contraindications. Agreeing with Feldweg,[8] we do not use evipal on asthmatics.

Provided the potential dangers are appreciated and proper caution observed, however, we do not consider the sitting position an absolute contraindication to evipal any more than to avertin, which also causes a fall in blood pressure and depresses the respiratory center. Also, although we do not use barbiturates as a routine preoperative medication, on a number of occasions we have supplemented spinal anesthesia by evipal, although large amounts of luminal had already been given. No alarming reactions or difficulties were encountered. If the fractional method of administration is used, we see no reason why premedication with barbiturates should constitute an absolute contraindication to evipal.

INDICATIONS

Evipal has been hailed as the ideal anesthetic for surgical procedures which can be completed within fifteen or twenty minutes. Although it has proved preeminently satisfactory from the patient's viewpoint, it is far from being an ideal anesthetic. The fact that it is an intravenous anesthetic, and that once administered its action is irrevocable; the recognized uncertainty of its action based, perhaps, on individual idiosyncrasies to the drug; the occasional difficulty of venipuncture in obese patients; the long recovery period, if the operation is prolonged; the depression of respiration; and the necessity of having an anesthetist in addition to the one administering the drug, frequently have induced us to prefer nitrous oxide.

On the other hand, we feel that the scope of evipal anesthesia may be extended to operations which may require thirty to forty minutes or even longer for their completion, and we feel that the singular qualities of evipal make it the anesthetic of choice for many operative procedures. Notably among these are the supplementing of spinal or local anesthesia, certain operations on the head or face, the closure of disrupted wounds, and operations under circumstances in which cumbersome apparatus or means of restraining the patient during induction are not easily obtained.

The smoothness and rapidity of evipal induction renders it the anesthetic of choice to supplement spinal or local anesthesia on patients in

good general condition. The change from a failing or incomplete spinal to general anesthesia can now be accomplished without the distressing struggle and disruption of the operative field which so often accompanied the change to ether or gas oxygen. Moreover, it is often surprising how long a spinal anesthesia can be supplemented by the use of only a few cubic centimeters of evipal. Combined with local anesthesia, evipal has proved equally efficacious. Thus, for example, in patients in whom a prolonged general or spinal anesthesia is inadvisable, the abdomen may be opened under local anesthesia, a few cubic centimeters given to permit excision of a bladder tumor, or enucleation of an enlarged prostate, and then the closure completed under local anesthesia.

For operations about the head and face, evipal is indeed ideal. It has been used extensively at the Peter Bent Brigham Hospital for dental work, including the reduction and wiring of fractured jaws. At the Beverly Hospital it has been used frequently in operations on the antrum, where it possesses the advantage that, although relaxation of the jaw is satisfactory, the cough reflex is usually preserved, preventing aspiration of foreign material. This preservation of the cough reflex, however, renders evipal somewhat less satisfactory for bronchoscopy and esophagoscopy than other anesthetics. Evipal has become practically the standard anesthesia at the Peter Bent Brigham Hospital for the incision or excision of large carbuncles of the neck, formerly always an annoying procedure under gas oxygen. It has also proved a great boon in the treatment of severe burns or lacerations of the face, requiring a general anesthetic for débridement and cleansing. It should be noted, however, that the enthusiasm for evipal in operations about the head and neck must not be extended to the treatment of deep cervical phlegmons, where any general anesthesia which relaxes the muscles of respiration and deglutition is dangerous.

Rapidity and ease of induction also makes evipal very satisfactory in the treatment of a disrupted wound. We have had two occasions to use it for this purpose, and not only has the relaxation been satisfactory, but the remarkable absence of struggling or straining during the induction has made what ordinarily is a most trying situation a comparatively easy one. It may be argued that the action of evipal is not sufficiently reliable to permit its use in so critical an emergency as a disrupted wound, but provided preparations are made to supplement with an inhalation anesthetic if necessary, this objection is not a valid one. Moreover, patients with disrupted wounds are often in rather poor general condition, and should require comparatively little evipal to obtain and maintain satisfactory relaxation.

Finally, under circumstances in which cumbersome apparatus, or means of restraining the patient during induction, are not easily ob-

tained, evipal is of great advantage. The question naturally arises as to whether or not evipal should be used in the office or home. Provided the necessary personnel to care for the patient and a supply of oxygen and carbon dioxide is available, this is permissible, and as knowledge of the drug increases, it may be used as freely in office practice as gas oxygen. At present, however, we would deprecate its use under circumstances in which a supply of oxygen and carbon dioxide, and an anesthetist in addition to the one administering the anesthetic are not available. Indiscriminate employment of the drug in our present state of knowledge may readily lead to fatalities which will discredit what seems to be a valuable adjunct to our anesthetic armamentarium.

SUMMARY

1. A clinical study of three hundred evipal anesthesias is presented.

2. Certain dangers and contraindications are discussed. The importance of individualization in the use of this new anesthetic is emphasized.

3. A technic of administration is given and particular indications for this type of anesthesia are outlined.

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BLOOD CONCENTRATION PRODUCED BY PLASMAPHERESIS

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SEVERAL workers have reported that in certain experimental or clinical shocklike conditions, there is an extensive loss of plasmalike fluid into a locally traumatized area. These authors have concluded that in many instances the amount of this fluid loss is sufficient to account for some of the symptoms present, and in certain cases to explain the resultant death itself. Analyses of the exudates have shown them to be similar to blood plasma in chemical composition, especially as regards protein content. Loss of such plasmalike fluid has been reported in burns,[1-3] freezing,[4] bile peritonitis,[5] tissue autolysis in vivo,[6] pneumonia and pulmonary edema,[7] portal and mesenteric obstruction,[8] and following release of an extremital constrictor.[9]

The question naturally arises as to whether the amount of such fluid lost from the circulating blood stream in these cases is sufficient to account for the morbidity and mortality involved. The amount of blood which will produce death when lost from normal animals has been differently reported by various observers. Boyce, Lampert, and McFetridge[10] reported that dogs could be bled 4.6 per cent body weight without shock or death resulting. Roome, Keith, and Phemister[11] reported that 4.5 per cent blood loss would produce death in dogs, and Johnson and Blalock[12] found the same figure to be 5.1 per cent. Elman and Cole[8] found that death followed a 2.7 per cent loss of blood from hemorrhage in normal cats. Evidence obtained from plasmapheresis experiments indicates that experimental animals cannot tolerate the loss of plasma as well as whole blood. These latter experiments are open to the objection that the reinjection of centrifuged cells after the removal of plasma may introduce factors that must be reckoned with besides the plasma loss. The centrifuged cells even if not hemolyzed may hasten the occurrence of death in an already weakened animal. Johnson and Blalock[12] found that dogs would die after loss of varying amounts of blood plasma by plasmapheresis dependent on the time interval. When the blood plasma was removed in amounts equalling 0.5 per cent body weight at hourly intervals, the total amount removed in percentages of body weight varied from 2.5 per cent plasma and 1.0 per cent whole blood to 3.5 per cent plasma and 0.85 per cent

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whole blood. The average sum of these figures was 4.05 per cent which was the average total loss of plasma and whole blood. The figure for the whole blood is necessarily included, because the animals died before the red blood cells from the last bleeding had been replaced. The average increase in hemoglobin was 34 per cent of the control figures. When the bleedings were performed at six-hour intervals, the average loss was 2.4 per cent plasma and 0.2 per cent whole blood. The sum of these figures is 2.6 per cent which was the average total loss of plasma and whole blood. The average increase in hemoglobin was 24.0 per cent of the control figures.

Roome, Keith, and Phemister[11] found that an average plasma loss of 3.0 per cent body weight in a series of five dogs would reduce the blood pressure to a shock level. These authors found the terminal blood loss in this series to be 1.4 per cent body weight. This makes the total plasma and blood loss 4.4 per cent. The blood was concentrated by this procedure, but no figures in this regard are given in the report. The authors state that removal of less plasma than whole blood would produce death.

The amount of plasmalike fluid lost in various shocklike conditions has been found by various observers to be of the same order of magnitude as the figures quoted in the previous paragraph. This makes them of especial significance, and one of the purposes of this paper is to check them under slightly different circumstances. The maximal blood concentration producible by plasmapheresis has also not been thoroughly studied heretofore.

EXPERIMENTAL

Dogs under barbital anesthesia were used throughout. Blood was withdrawn from one femoral artery into centrifuge tubes containing sodium citrate, and after centrifuging and removal of the plasma, the cells were reinjected into the opposite femoral vein. In certain experiments this was done using aseptic surgical technic, in others only chemical cleanliness was employed, and the results in the two groups showed no marked difference. The blood pressure was recorded by means of a cannula inserted into the right carotid artery connected to a recording drum. Hemoglobin (Sahli) and hematocrit (Van Allen) determinations were made as controls and during the course of the experiment. Bleeding was performed at usually half-hour intervals or longer, and as the blood pressure fell, smaller and smaller amounts of blood were removed, so that the last lethal sample would be as small as possible. After centrifuging, the cells were reintroduced without dilution. The results of eight experiments are given in Table I. It is seen that the amount of plasma removed averaged 4.0 per cent

body weight and that the amount of blood at the terminal bleeding averaged 0.4 per cent, the total being 4.4 per cent. The average time from the first to the last bleeding was ten and one-half hours.

In Experiment 6, with 7 bleedings totalling 2,500 c.c. and following centrifuging, 1,075 c.c. of plasma were removed. Eighty c.c. of the 1,425 c.c. of cells were lost and not replaced. The last bleeding was done ten hours after the first, and after reintroduction of the cells, 300 c.c. of plasma were slowly reinjected intravenously over a period of fifty minutes. The blood pressure was 86 mm., or lower, beginning three hours after the first bleeding, except for a four-minute period when it rose to 112 immediately after reinjection of cells before the plasma infusion was begun. The plasma infusion had practically no effect on the blood pressure which fell to 46 nine hours later. The dog died about 20 hours after the first bleeding.

The average hemoglobin percentage in all the experiments before the plasmapheresis was begun was 95, and the final reading was 147. The initial and final hematocrit readings were 49 and 69 respectively. This represents an increase of 55 per cent over the control reading for the hemoglobin and 41 per cent for the hematocrit.

COMMENT

The unsuccessful attempt to restore one of the animals by reinjection of the removed plasma is in accord with attempts to treat some other types of plasma loss.[5] No further discussion of this point will be made in the present paper. The amount of blood concentration obtained by radical plasmapheresis was found to be 55 per cent by hemoglobin estimation and 41 per cent by the hematocrit reading. No especial significance is attributed to the difference in these averages. Possibly with plasma depletion, the cells lost water to the surrounding substrate and shrank. This would account for the greater increase in hemoglobin than hematocrit readings. The average increase in blood concentration of about 50 per cent of the control reading is greater than that found by Johnson and Blalock[12] (24 to 34 per cent).

Johnson and Blalock's experimental observation that a smaller amount of plasma would kill when removed slowly than when removed rapidly is of interest. In our experiments, the time between the first and last bleeding varied from four hours to twenty hours, and no especial difference was noted in the lethal amount of plasmapheresis. It is possible that once the blood pressure has been lowered, the longer it is allowed to remain at a low level, the more precarious the state of the animal becomes and the less plasma needs to be removed later to produce death. This affords a possible explanation for Johnson and Blalock's results. It is also possible that the prolonged anesthesia

TABLE I

RESULTS OF PLASMA REMOVAL IN EIGHT ANIMALS

In Most Instances the Final Blood Pressure, Hemoglobin, and Hematocrit Readings Were taken Just Before the Final Bleeding

EXP. NO.	BLOOD PRESSURE		HEMOGLOBIN		HEMATOCRIT		DOG WEIGHT KG.	NO. OF BLEEDINGS	INTERVALS IN HOURS FROM FIRST TO LAST BLEEDING	PLASMA REMOVAL PER CENT BODY WEIGHT	BLOOD REMOVED TERMINALLY PER CENT BODY WEIGHT	TOTAL AMOUNT PLASMA PLUS BLOOD REMOVED TERMINALLY PER CENT BODY WEIGHT
	INITIAL	FINAL	INITIAL	FINAL	INITIAL	FINAL						
1	150	56	100	145	53	69	9.3	6	4	3.5	0.0*	3.5
2	120	60	89	148	45	68	9.8	7	9	4.2	0.0	4.2
3	156	70	102	152	44	64	10.4	3	7	3.0	0.8	3.8
4	148	40	77	121	33	56	15.4	7	4½	4.5	0.4	4.9
5	140	48	92	130	62	72	27.0	7	20	3.8	0.5	4.3
6	152	44	92	142	47	66	19.0	7	10	5.6	0.0	5.6
7	116	78	106	168	49	75	13.0	10	10	4.6	0.0	4.6
8	140	68	101	167	57	81	21.5	9	19½	2.8	1.1	3.9
Average	144	58	95	147	49	69	15.8	7	10½	4.0	0.4	4.4

*In the experiments in which no blood was removed terminally, death occurred between bleedings and after the final red cell reinjection.

may have been a factor. Seeley, Essex, and Mann[15] have studied the relation of various types of anesthetic agents to the development of traumatic shock.

The amount of plasma removed in the eight experiments averaged 4.0 per cent body weight. This is considerably more than removed by Johnson and Blalock[12] in the plasmapheresis experiments previously cited. It is of interest that it is also more than has been reported in various other shocklike conditions: burns, 3.2 per cent (Blalock[2]), 2.2 per cent (Harkins[3]); freezing 2.6 per cent (Harkins, et al.[4]); release of an extremital constrictor, 3.5 per cent (Wilson and Roome[9]); bile peritonitis, 2.5 per cent (Harkins, et al.[5]); and intestinal manipulation, 4.5 per cent (Blalock[13]). With the exception of the fluid recovered in experiments on manipulated intestines, these figures are less than the amount of plasma which when removed by plasmapheresis will be fatal. The blood concentrations reported in several of these conditions, however, are as great as the maximal concentration produced by plasmapheresis. Moon[14] has reported extensive blood concentration in several shocklike conditions, and it is possible that in them there is a general leakage of fluid from the capillaries all over the body, as well as at the site of the local lesion. Hence in these instances, the local loss of fluid may not be the only lethal factor and may not be the cause of all the blood concentration. In plasmapheresis on the other hand, especially when done rapidly, it seems likely that the plasma directly removed is the cause of most, if not all, the blood concentration and accompanying blood pressure fall.

SUMMARY AND CONCLUSIONS

1. The amount of plasma which, when removed from experimental animals, will produce death was 4.0 per cent body weight. This is more than the local fluid loss reported by various observers in other shocklike conditions, as well as following plasmapheresis itself.

2. The amount of blood concentration producible by plasmapheresis was not found to be greater than that in certain other shocklike conditions. It is possible, therefore, that in the latter there may be a generalized as well as a local fluid loss.

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PERSISTENT HYPERTENSION DUE TO HYPOTHALAMIC INJURY

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PERSISTENT elevation of the systolic blood pressure in experimental animals as the result of renal ischemia has recently been demonstrated by Goldblatt, et al.[1] This communication presents some observations on a canine with a resultant hypertension due to direct injury to the hypothalamus. The marked rise in systolic and diastolic blood pressure was discovered during routine postoperative studies on animals which had been subjected to procedures intended to produce diabetes insipidus. The hypothalamic area in a normal, mature, male beagle hound was exposed by the technic described by Crowe, Cushing, and Homans.[2] A three-millimeter transverse incision was made immediately posterior to the infundibulum, sufficiently deep to puncture the third ventricle in the midline. Five weeks following injury to the hypothalamus, the blood pressure had risen from a normal level to 242/130. Bradycardia was associated with the hypertension. As this phenomenon was striking, the animal was studied for a period of five months. During this time, the blood pressure remained persistently elevated. There were obvious pulsations of both axillary and femoral vessels. The femoral artery, on palpation, had a resounding snap, although no actual change in the vessel wall could be ascertained. There were no pulsations of the vessels in the eyegrounds, but increasing tortuosity and A-V nicking developed. No hemorrhages appeared in the fundi. Exercise augmented the pulse rate but slightly from a level of 88 to 100. There was a faint systolic whiff heard best over the base of the heart. Roentgen examination of the heart revealed evidence of cardiac enlargement of 23 per cent over a period of four months. No disturbance of carbohydrate or water metabolism developed. For purposes of comparison, blood pressure responses to various stimuli were carried out on canines with hypertension due to renal ischemia and on normal controls.

From Table I it can be seen that the animal with hypothalamic injury showed a more labile response to various stimuli. The increase in pulse rate under nembutal anesthesia has not been explained. The dog with hypertension due to renal ischemia showed a more fixed type of hypertension, with but slight change under nembutal anesthesia or fol-

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lowing various stimuli. Further clinical pathologic studies and necropsy reports of animals with experimental hypothalamic hypertension will be submitted.

TABLE I

BLOOD PRESSURE RESPONSES IN HYPERTENSIVE AND NORMAL DOGS TO VARIOUS STIMULI

TEST	NORMAL DOGS		GOLDBLATT DOG		DOG WITH HYPOTHALAMIC INJURY	
	B. P.	PULSE	B. P.	PULSE	B. P.	PULSE
Test	136/ 83	110	200/120	118	242/130	80
Exercise	182/115	132	210/128	120	290/148	91
Nembutal anesthesia	90/ 70	84	190/110	90	120/ 60	110
Water at 5° C.	204/122	130	202/124	128	300/140	100
Insulin hypoglycemia	178/110	Variable	230/130	Variable	290/175	Variable

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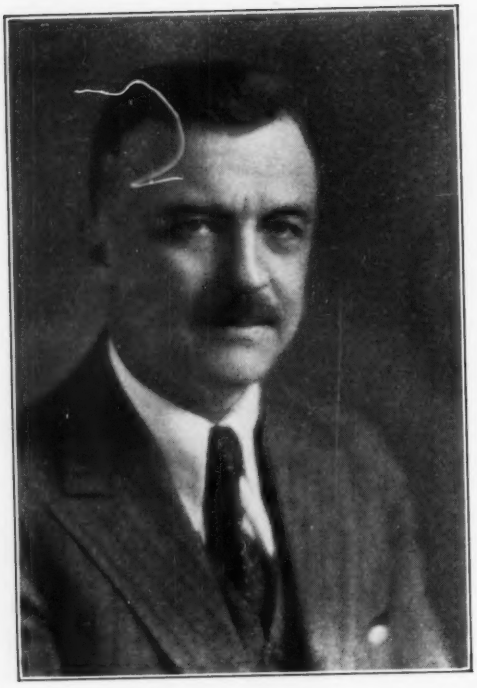

Howard L. Beye
1886-1936

In Memoriam

HOWARD L. BEYE
1886-1936

THE surgical profession has lost one of its brilliant younger members by the untimely death of Howard L. Beye, professor of surgery at the University of Iowa, who was killed in an automobile accident near Marshalltown on September 29, 1936.

Dr. Beye was born at Oak Park, Ill., on September 24, 1886. He graduated from the University of Wisconsin in 1909, and received his degree in medicine at Rush College in 1911. During the following year and a half, he served as interne at Cook County Hospital, and at once began teaching as an assistant in medicine at Rush. In 1914, he came to Iowa City as an instructor in surgery at the Medical School of Iowa State University under his friend and teacher, Dr. Charles Rowan. He was appointed professor of surgery in 1924, and three years later succeeded Dr. Rowan as active head of the surgical department. He served overseas during the World War and was wounded in action at Chateau Thierry. Shortly after returning to Iowa City, he was married to Ruth Ketcham of Oak Park, and to them have been born six children, four girls and two boys.

Dr. Beye's work in the field of surgery has won for him wide recognition and fellowship in outstanding societies. He was a member in good standing in the Johnson County Medical Society, the Iowa State Medical Society, the American Medical Association, the American College of Surgeons, the Western Surgical Association, the American Association of Thoracic Surgery, and the American Surgical Association. Some weeks before his death, Dr. Beye had consented to accept a place on the Committee on Publications of SURGERY.

Dr. Beye had a wide interest in the field of general surgery, as can be seen from the diversity of his contributions to surgical literature during the past twenty years, but unquestionably his chief interest of late has been in the diseases of the thorax. I know of no better way of paying adequate tribute to his work and character than by quoting from a personal letter which I received a few days ago from his associate of many years, Dr. Frank Peterson, now head of the department of surgery at Iowa City: "His particular interest, as far as surgery was concerned, had been in diseases of the thorax. He had been spending innumerable hours in study and in the laboratory improving his knowledge of the anatomy, particularly as related to the lung and mediastinum. Just a few weeks prior to his death he had done a masterly pneumonectomy for carcinoma of the bronchus, with remarkably little postoperative reaction. That the patient died later from an unexpected complication was a terrible blow to him. His passing has left a terrific void for those of us who have worked with him these many years. There is nothing which can be said about him which will in any way overemphasize his ambition, his honesty, and his straightforwardness."

EDWIN N. MILLER.

Editorials

What Is Minor Surgery?

WHEN it is remembered that principles are to guide us in surgical practice and that success in applying these requires always discriminating judgment and a certain aptitude, it seems useless to create a division of surgery into major and minor—or, rather, to set apart so-called minor surgery as a special department. But this artificial division has come about in some way and has gradually assumed a popular position without, it is feared, a good reason for its existence. To seek a proper definition of minor surgery, to point out, if possible, its boundary lines, to call attention to the misconceptions and dangers which may arise from regarding it as a separate branch of surgery—these appear to be pertinent objects.

One looks in vain for a definition of minor surgery which really defines. Search of textbooks and other literature shows a hopeless lack of uniformity, even of subjects embraced under the term. The definition given by Gross in 1882, which is the clearest to be found at that period, differs widely from the modern meaning. He calls minor surgery "an account of some of the more common instruments used in surgery, of the mode of making incisions, or of performing the elementary operations, the establishment of issues, the introduction of the seton, the application of the cautery, bleeding, and the art of bandaging and dressing." Besides these subjects, some of which are now obsolete, Gross discusses in the same chapter aspiration, skin and sponge grafting, transfusion of blood, hypodermic injections, vaccination, counterirritation, antiseptics, electricity, and massage. John Ashhurst (1889) has about the same subjects in his chapter on minor surgery. So does the *American Text Book of Surgery* (1892), which adds remarks on the clinical thermometer, heat and cold, adhesive plaster, and collodion. How different from the more recent conceptions of minor surgery!

Of the newest books on surgery in general, practically none contains a specific reference to, or has a chapter treating of, this subject. There are, however, several special works on minor surgery, small and large. It is interesting to compare the contents of these volumes with the very different ideas on the subject which existed even twenty years ago. Most of the works on minor surgery published as late as forty years ago were largely taken up with bandaging. One of the oldest is by

Wharton; yet in the book, he gives no definition whatever of minor surgery. Furthermore, the last edition included fractures and dislocations, ligation of arteries, amputations, excisions, operations on nerves, removal of the vermiform appendix, lithotomy, cholecystostomy, and gastroenterostomy. If this be minor surgery, make the most of it!

The extensive treatise of Foote, with its 752 pages, shows a better spirit, in that the reader is now and then referred to textbooks on "major surgery." Its contents are carefully chosen. But the author does not tell us what minor surgery is.

Of the newest books, one (1935) discusses fracture of the skull; surgery of the nasopharynx, neck, jaws, and chest, with directions for operation in such conditions; diseases of the male and the female genital organs and of the extremities. Neither the eye nor the abdominal cavity are considered; hernia is described in detail. How much of this is major surgery?

A book (1935) of almost a thousand pages, which has gone through three editions, follows about the same table of contents as the work mentioned above. In the preface to the first edition (1929), the subject is defined as follows: "Minor surgery is the surgery which has a low mortality; which requires but few assistants; which generally is done in the hospital out-patient department or in the office. It includes the large majority of surgical cases; the everyday surgical conditions. *All minor surgery potentially is major surgery; often a distinction cannot be made.*"* Without disparaging the methods of treating the subjects or the value of the volume as a book of instruction (it is really an excellent and thorough treatise), objection must be made to the title.

Moreover, the definition will not hold water. Most all our surgical operations have a low mortality; many can be done with "but few assistants;" some must be done, even so-called major operations, as emergencies in hospital dispensaries and in the office. If minor surgery "includes the large majority of surgical cases," where do our major surgical cases come in? Finally, the author admits that "often a distinction cannot be made," because "all minor surgery is potentially major surgery." It is unfortunate that one should attempt to make the distinction.

To show my admiration for this author as a teacher and writer, I have endorsed the larger work (*Text Book of Surgery*, 1936), so ably edited by him, and regard it as the best book of its kind now extant. His book on *Minor Surgery* might be considered as the first volume of a combined work. The truth is, it requires much more knowledge and skill to perform many operations customarily classed under the head

*The italics are Dr. Royster's.

of minor surgery (plastic operations, for example) than it does to execute certain procedures listed by some of our institutions as major surgery.

Now, the question naturally arises, where is the dividing line? Where does minor surgery end and major surgery begin? Or, if you please, where is the field of the term, major surgery, and who will essay a definition of that? If there is a major and a minor surgery, should there not be a superlative degree—a supreme surgery? The careless regard for terms, the tendency of authors and teachers to neglect what they would consider the smaller matters, and the encroachments of textbooks of minor surgery, together with hazy and diverse ideas in the minds of individuals, have served to render the classification difficult or even impossible. Indeed, it appears that the only proper basis for distinction between a minor and a major surgical operation depends upon the one who does it. A definition might be made as follows: *Minor surgery is that part of surgical practice which is done by the "minor surgeon."* The "major surgeon" also does what is included under minor surgery, though refusing to call it by that name; but the "minor surgeon" does not and should not do major surgery. Herein lies the danger. There is hardly a so-called minor operation which may not become a major one at any moment, and the more "minor" the surgeon, the more "major" the operation will become before he is through with it. The experienced surgeon does not try to locate the line of demarcation.

Curettage, an operation for hemorrhoids, aspiration for empyema, and the open treatment of fractures and dislocations will be undertaken by those who would not think of performing an abdominal section, the resection of a rib, or the formal ligation of an artery. And yet, in each of the operations first mentioned, there is the possibility of having to do one of those operations last named. Equal skill is required for both these classes of operating, but in the latter there are elements of risk, immediate and remote, which deter the average man from attempting what are called major operations. It is sometimes a matter of "nerve," and "nerve" means simply knowing what you are doing. In surgery, familiarity breeds repose.

It is by no means contended that the general practitioner should not do surgery; it is even urged that he do more and more, so that he may become proficient in that which falls to his lot, and not shirk his responsibilities. He should, however, understand deeply that the study of surgical principles is his duty, that surgery is the same wherever it is needed, that none of it is minor, and that all of it is surgery. Let him tune his judgment to his conscience, realize his limitations (as everyone must), and do surgery, not minor surgery.

The strangest feature of the minor surgery propaganda is that such a division has no counterpart in other branches of medicine. We have heard nothing of minor medicine, minor obstetrics, minor neurology. Why not separate the big from the little things in these specialties? The wave has struck the diseases of women, and there has resulted the term, "medical" gynecology—whatever that may mean. These dissociations are not for the clearing up of the subject; rather they tend to the confusion of it.

When all is said and done, the question of what shall be considered as minor surgery is a matter of individual opinion. What one would regard as properly included under this arbitrarily erected department of surgery, another might consider as belonging to the larger subject alone. Such disagreements were manifest on asking the question of many professional associates, the replies varying from those who thought minor surgery to be that which was done without a general anesthetic, up to those who classed it as the performance only of those operations which are not per se dangerous to life. Most of us cannot define the subject to our own satisfaction, much less to that of others. It is not necessary to define it, or to set its boundaries, if we shall here apply the precept furnished by two important truths: the greater includes the lesser, and a chain is no stronger than its weakest link.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

RECENT ADVANCES IN NEUROSURGERY

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Part II*

V. CONGENITAL DISORDERS AND THE SPASTIC STATES

THE disorders to be discussed in this section have long been a *bête noir* to the neurosurgeon, and though recent progress gives promise of improvement, they are still among his most difficult problems.

Since the beginnings of medicine, the distressing problem of hydrocephalus has defied solution (cf. Weed,[187] and Cushing[188]). Until recent years, most operations designed for the relief of the "communicating" type had as their aim the release of dammed-up cerebrospinal fluid through some type of fistula, under the skin, into the retroperitoneal tissues or into a ureter. These early methods have been discussed in a paper by Davidoff[189] whose ingenious experimental skin-tube operation has not apparently been given a clinical trial. More recently, surgical efforts have been directed toward diminishing the production of cerebrospinal fluid by removal of the choroid plexuses from the lateral ventricles. This may be done through a small cortical incision (Dandy[190]). The ventriculoscopic approach originally employed by Dandy,[191] and Mixter [192] has been used recently by Putnam,[193, 194] and Scarff[195] for electrocoagulation of the choroid plexus, with very satisfactory results.

On the other hand, the "obstructive" type of hydrocephalus (i.e., the type in which the obstruction lies within the ventricular system or at its outlet) may be treated either by attacking the obstruction directly (Dandy[196, 197]), or by providing a new cerebrospinal fluid outlet through the floor of the third ventricle† (Dandy,[190, 198] Mixter[192]).

It is important to remember that any operation for hydrocephalus must be undertaken before extensive cerebral damage resulting from prolonged compression has occurred.

A somewhat less gloomy picture is presented by the plastic operations for spina bifida and cranium bifidum. These congenital bony defects allow the protrusion of meningeal sacs containing cerebrospinal fluid with or without portions of the spinal cord, cauda equina, or brain.

*Part I of this paper appeared in the January issue of SURGERY.

†In 1909, Von Bramann[199] performed puncture of the corpus callosum for the same purpose, but the method has met with little success.

Encouraging series of such cases have been reported by Gross and Sachs,[200] Jelsma and Spurling,[201] and Penfield and Cone.[202, 203] The last named authors attach great importance to the preservation of the sac as a means of preventing the subsequent development of the hydrocephalus which frequently follows these operations.

It is convenient to include in this section the great groups of cases of spasticity, athetosis, and related disorders, although, of course, many of these are not congenital, and, indeed, their etiology is often a matter of controversy. They have in common, however, the fact that all are disorders of the mechanism of movement.*

Little or no progress has been made in the treatment of the purely spastic disorders (e.g., Little's disease), although it is well to remember that Royle's pioneering sympathetic ramisectomies,[209, 210] undertaken for the treatment of spasticity, helped to popularize a great new field of neurosurgery (cf. Section X). Further, some of these distressing cases probably result from birth injuries and may be prevented by prompt treatment immediately after birth (Munro[211]).

On the other hand, interest in the surgical relief of athetosis and the dystonias has been reawakened by recent neurophysiologic discoveries (Section I, frontal lobe). In 1932, Bucy and Buchanan[212] reported resection of portions of the premotor and motor cortex for athetosis of one arm, with complete cessation of the athetoid movements. Sachs,[213] in 1935, reported three cases of athetosis treated by "subpial resection of the cortex," an operation originally employed for the same purpose by Horsley[214] in 1909. From Sachs' description, it seems probable that portions of both motor and premotor areas were included in the tissue removed. The results were very satisfactory. A case having a resection confined to the premotor area by Pilcher[215] had a recurrence of athetoid movements several weeks after the almost immediate return of voluntary motion.

Meantime, Putnam[216] devised an operation for athetosis which consisted of section of the anterior or anterior and lateral extrapyramidal tracts high in the spinal cord. In four cases (two of postencephalitic athetosis and two of familial dystonia musculorum), considerable improvement resulted, while in two cases of paralysis agitans, slight improvement occurred in only one. Oldberg[217] has used a similar operation for athetosis with satisfactory results in some cases.

Spasmodic (or spastic) torticollis is another disorder of movement whose somatic etiologic aspects bring it into the group under discussion. However, in almost all, if not all, cases, there is an additional psychomotor element which plays a large part in its symptomatology as well as in the therapeutic results. Space does not permit a discussion of this

*It seems probable on experimental and clinical grounds that the lesions of all of the amyostatic disorders involve to a greater or lesser extent the extrapyramidal motor system (cf. Foerster,[204, 205] Jakob,[206] the papers of Fulton and his associates presented in Section I, and the papers cited in the following paragraphs). This hypothesis, however, must not be accepted as conclusively proved (Wilson [207, 208]).

interesting phase of the subject. The reader is referred to the papers of Foerster,[204] Hassin,[218] Grinker and Walker,[219] and those presently to be cited.

The early operative treatment of spasmodic torticollis was directed locally toward the sternocleidomastoid and associated muscles or the accessory nerves. It was gradually realized, however, that the deeper and more posterior muscles of the neck were involved, and extravertebral section of the upper spinal nerves was then advocated. Keen[220] first performed this operation in 1891, and there were no further innovations until 1924, when McKenzie[221] reported section of the upper three cervical anterior and posterior roots and spinal accessory nerves intradurally, on one side, by Cushing. The patient was greatly improved. McKenzie expressed the opinion that the anterior roots could probably be spared without impairing the result. Foerster[222] had performed essentially the same operation four times in 1926 and, in 1929, he[223] advocated section of only the posterior roots.

Finney and Hughson[224] first realized that the disease is always actually or potentially bilateral and performed extravertebral section of the first three cervical nerves on both sides, with improvement in all but three of thirty-two cases (1925). The operations of Frazier,[225, 226] and Dandy,[227] both introduced in 1930, differ in that the former advocates bilateral section of the posterior roots of the first three cervical nerves, while the latter at first advised section of both anterior and posterior roots, but subsequently[228] of only the anterior roots of the same nerves. The two operations probably produce equally satisfactory results, and the choice depends upon whether one prefers the anesthesia or the motor paralysis (for which the unparalyzed muscles soon largely compensate).

VI. INJURIES AND INFLAMMATIONS

Injuries of the head and spine grow more numerous each year with the increase in accidents resulting from rapid automobile travel, and they constitute an increasingly common problem for general practitioner and neurosurgeon alike. Many important contributions to the subject have been made, but there is as yet no unanimity of opinion regarding the therapy of head injuries.

Following the demonstration by Weed and his associates,[229-232] in 1919 and 1921, of the reduction in cerebrospinal fluid pressure and in the bulk of the brain which follows the intravenous administration of hypertonic solutions, the use of these solutions and of other "dehydrating" methods has been widely advocated. The chief exponent of the dehydration therapy has been Temple Fay, who has written numerous papers on the subject. These are summarized in a recent publication.[233]

Another widely used method of treatment is that of frequent lumbar punctures for the relief of cerebral compression and the removal of blood

from the subarachnoid space; Munro,[234] reporting 1,494 cases, believes this the most effective treatment and has repeatedly insisted upon its superiority.[235, 236]

On the other hand, there is a considerable weight of opinion opposing both of these therapeutic methods. On clinical grounds, Sachs[237, 238] condemns spinal puncture as too dangerous, and the method is also opposed by Coleman,[239] and Dandy.[240] The latter also feels that the use of hypertonic solutions is unwise[241] and believes that subtemporal decompression should be employed in many cases. Experimentally, Sprong[242] has shown that the rate of disappearance of blood in the cerebrospinal fluid is not affected by withdrawal of fluid, and Masserman's[243-247] studies indicate that the rapid reduction of cerebrospinal fluid pressure by either intravenous injection of hypertonic solutions or lumbar puncture is likely to be followed by a secondary rise in pressure beyond the original level. This evidence is in confirmation of the previous observations of Haug.[248] Recently hypertonic solutions of sucrose have been investigated (Bullock, Gregerson, and Kinney,[249] and Masserman[250] and give promise of being more satisfactory than dextrose.

This important controversy has been reviewed in a recent comprehensive paper by Lehman and Parker,[251] who point out how little is really known regarding the mechanism of the changes following head trauma. In a valuable experimental study, the same authors[252] have shown that the increased pressure following replacement of cerebrospinal fluid by blood is probably the result of the increased osmotic pressure of the cerebrospinal fluid. Considerable doubt is thrown upon the existence of "traumatic cerebral edema" (i.e., increased tissue fluid) by the experiments of Pilcher,[253] and the postmortem observations of Connors and Wright.[254]

The literature on wounds of the brain has been recently reviewed by Pilcher,[255] whose experimental study demonstrated the dangers of retention of foreign bodies, contamination of the ventricles, and failure to treat cerebral wounds promptly. An excellent clinical paper on compound fracture of the skull has been published by Munro, [256] and Naffziger and Glaser[257] have studied depressed fractures in rabbits. The histologic aspects of head injuries have been extensively studied by Rand and Courville,[258-262] and others (cf. Sections IV and IX).

Among the complications of head injuries, subdural hematoma has received considerable attention. Until very recently, these expanding lesions have been thought to increase in size by continuing venous bleeding (Putnam and Cushing,[263] Keegan,[264] Leary[265]). However, McKenzie,[266] and Gardner[267] believe that the hematoma sac acts as a dialyzing membrane, permitting fluid to be drawn into the sac by osmotic pressure, and a careful study by Munro and Merritt[268] seems to confirm this opinion. In 1932, McKenzie,[266] and Fleming and Jones[269] advised evacuation of the hematoma sac, rather than the more extensive osteo-

plastic exploration formerly employed. Furlow[270] believes this method is applicable only in selected cases, an opinion previously expressed by Rand.[271]

In this connection should be mentioned the important operative treatment of spontaneous cerebral hemorrhage, originally carried out by Cushing,[272] and Russell and Sargent[273] and recently revived by Penfield,[274] and Craig and Adson.[275] When employed in selected cases, the evacuation of the clot has been found to be a lifesaving measure.

Three important contributions to the treatment of spinal injuries are the traction-manipulation reduction of dislocations of the cervical spine by Taylor,[276] and Brookes,[277] the skeletal traction of Crutchfield,[278] and McKenzie,[279] and the method of tidal drainage of the bladder devised by Munro.[280]

Kahn[281] has had very satisfactory results in treating brain abscesses by allowing their spontaneous extrusion through an overlying skull and dural defect, and Fincher[282] has reported success with very radical bone removal for osteomyelitis of the skull. The rarity of successful open drainage of pyogenic meningitis (Ruttin,[283] Walker and Bucy[284]) emphasizes the discouraging status of the treatment of infections of the central nervous system.

VII. NEOPLASMS

Advances in our knowledge of the diagnosis and treatment of brain tumors have come largely through studies of large series of cases. Many of these were referred to in the section on neuropathology. Notable among numerous others are a series of studies of the meningiomas as they occur in various locations by Elsberg and his associates,[285-287] and Cushing and Eisenhardt;[288] of frontal lobe tumors by Voris, Adson, and Moersch,[289] Frazier,[290] Sachs,[291] Baruk[292] Vincent,[293] and Kolodny;[294] of intraventricular tumors by Dandy;[295, 296] of tumors producing unilateral exophthalmos by Elsberg, Hare, and Dyke,[297] and Voris and Adson;[298] of the acoustic tumors by Olivecrona;[299] of the pontine gliomas by Bailey;[300] and of the epidermoid tumors by Mahoney.[301]

The difficult problem of the proper treatment of the infiltrating gliomas of the cerebrum has been a controversial subject, particularly as regards the glioblastomas, probably the most rapidly growing of all brain tumors. There are three widely different opinions. In selected cases, Dandy,[302] and Gardner[303] have performed radical extirpation of entire right cerebral hemispheres (above the basal ganglia and thalamus). This formidable procedure, in addition to its operative risk, carries the certainty of leaving the patient a permanent invalid of greater or lesser degree, even if the tumor is completely eradicated. There are certainly few cases in whom it is justifiable.

Spurling,[304] however, feels that all patients in whom a glioblastoma is found should have only a wide subtemporal decompression for relief

of headache. The third opinion, that of McKenzie,[305] is that such cases should be given an "internal decompression" by removal of a portion of the tumor and should be spared the unsightly hernia and useless prolongation of life produced by subtemporal decompression.

On the other hand, the more benign gliomas (especially astrocytomas) should be radically treated by wide extirpation, lobectomy, or removal of the mural nodules of astrocytomatous cysts (Elsberg,[306] Frazier[290]).

Excellent general articles on brain tumors and pituitary tumors by McLean[307, 308] have just appeared in Bumke and Foerster's "Handbuch der Neurologie," and similar papers have been published in recent years by Foerster,[309] and Adson,[310] in addition to the texts and sections in systems of surgery to be mentioned in Section XI.

The results of operations for intracranial tumors have been brilliantly portrayed in several publications from Cushing's clinic. His statistical study of the operative results in over two thousand classified tumors,[311] with a total operative mortality of 11.9 per cent, ranks as a monument to the progress of neurosurgery. Similarly, the follow-up studies of Cairns,[312, 313] and Van Wagenen[314] have proved the ultimate usefulness of tumor removal.

The surgery of spinal cord tumors has long been well established. The sensory and motor "levels," with or without nerve root pain and bladder and bowel disturbances, the Queckenstedt test, the increased protein content of the spinal fluid (and its occasional xanthochromic color and spontaneous coagulation—the Froin syndrome), and the localization by injection of iodized oil, all combined to make the danger of incorrect diagnosis relatively small in most cases. Similarly, the treatment, especially of extramedullary tumors, is a satisfactory phase of neurosurgery. Numerous valuable papers, however, have appeared in recent years.

Harkins[315] has reviewed the still controversial question of the use of iodized oil and has pointed out its potentially harmful effects, but he confirms the generally accepted opinion (cf. Elsberg[316]) that it is indispensable in the diagnosis of otherwise unlocalizable tumors. Attention has recently been called to the spinal cord compression produced by rupture of the intervertebral disc with herniation into the canal by Peet and Echols,[317] Mixter and Barr,[318] Mixter and Ayer,[319] and Love and Adson.[320] It is now believed that many of the lesions formerly thought to be enchondromas were of this type. Elsberg, long a leader in the field of cord tumors, has continued to contribute to the subject,[316, 321, 322] and excellent general articles have been published by Ayer,[323] Spurling and Mayfield,[324] Learmonth,[325] Adelstein and Patterson,[326] Rogers,[327] Tamaki,[328] Grant,[329] and Kernohan, Woltman, and Adson, [330] among many others.

Irradiation therapy of the tumors of the nervous system and particularly of the gliomas has been extensively studied in recent years

and has yielded some encouraging results. The first roentgen treatment of brain tumors was reported by Nordentoft,[331, 332] and Christiansen[333] in Denmark in 1918. These papers were followed by those of Pancoast[334] in this country (1922), and Bremer, Coppez, and Sluys[335] in France (1923). Pancoast first observed that certain cerebellar tumors showed great improvement, and, after the gliomas came to be histologically classified, it was recognized that the cerebellar medulloblastomas are the most radiosensitive of all the gliomas (Bailey, Sosman, and Van Dessel,[336] Bailey[337]). The results with other tumor types are variable (Sachs, Rubinstein, and Arneson,[338] Dyke,[339] Olivecrona and Lysholm[340]). Recently, Davis and Cutler[341] have employed the actual implantation of radium into glioblastomas, and it is possible that the method may prove of value. Alpers and Pancoast,[342] and Bailey and O'Connell[343] have studied the effect of irradiation on brain tissue.

VIII. THE CRANIAL NERVE TICS AND THE RELIEF OF INTRACTABLE PAIN

When unbearable pain is of unknown or irremediable cause, symptomatic relief may usually be offered by interruption of the pain-bearing nerve pathways. This is the basis of one of the most satisfactory phases of neurosurgery.

Trigeminal Neuralgia.—With the introduction by Frazier[344-347] of the differential section of the trigeminal root, which leaves corneal innervation and the motor root intact, the treatment of trigeminal neuralgia was placed upon a firm and rational basis, and this operation is still the procedure of choice of most neurosurgeons. Dandy,[348] however, in 1925, began to do subtotal root sections in the posterior fossa, and has found this procedure satisfactory in a large number of cases.[349, 350] Klemme,[351] who uses the temporal approach, states that very accurate subtotal division of the root can be obtained by splitting the ganglion from a point between the origins of the first and second divisions of the nerve backward into the posterior root. Preliminary alcohol injection of the peripheral divisions of the nerve, as a diagnostic measure and to familiarize the patient with the numbness which will follow posterior root section, is strongly advised by Grant,[352] and by Horrax and Poppen,[353] but is opposed by Dandy,[354] and others.

Following its introduction by Härtel,[355, 356] the injection of the gasserian ganglion has been employed in Germany by Zander,[357] Stiasny,[358] and Sgalitzer and Brücke,[359] in England by Harris,[360] and in this country by Irger,[361, 362] and Putnam and Hampton.[363*] In 1933, Kirschner[364, 365] advocated coagulation of the ganglion by means of an electrode enclosed within a long needle which is inserted through the foramen ovale. This method has also been employed by Zenker.[366] It

*In a personal communication, Putnam states that he now prefers the electrocoagulation of Kirschner.

must be remembered that these methods may destroy the entire ganglion and the motor root, in addition to involving certain other dangers (cf. Putnam and Hampton[363]).

Section or injection of the trigeminal nerve afford equally complete relief for the pain of inoperable tumors in and about the mouth and face (Olivecrona,[367] Stiasny,[358] Putnam and Hampton,[363] and many others).

Glossopharyngeal Neuralgia.—The ninth cranial nerve is the seat of an excruciating neuralgia similar to that of the trigeminus, and intolerable pain in its distribution also often results from inoperable neoplasms. Glossopharyngeal neuralgia was first described in 1920 by Sicard and Robineau.[368] They sectioned the ninth nerve in the neck, an operation first performed a year earlier by Peet.[369] In 1924 Adson[370] suggested intracranial section, which was first done by Heath,[371] Fay,[372] and Davenport,[373] for the pain of inoperable tumors. Dandy[374] first treated true glossopharyngeal neuralgia by this method, and this operation is now the accepted procedure (Peet,[375] Filatov,[376] Keith[377]).

Ménière's Syndrome and Related Conditions.—It is convenient to consider here persistent vertigo and tinnitus, although it is by no means certain that they fall within the classification of cranial nerve ties. The etiology of Ménière's disease has been the subject of a number of recent observations. Some cases seem to be definitely allergic in character (Duke,[378] Proetz,[379] Urbach and Wilder[380]). On the other hand, Furstenberg, Lashmet, and Lathrop[381, 382] have concluded, after careful study of a number of cases, that the condition is due to excessive retention of sodium and have obtained remarkable results by restriction of sodium in the diet. Foldes,[383] and Bucy[384] report confirmatory evidence.

Meantime, after a number of sporadic surgical efforts,* a satisfactory operative treatment for intractable cases was firmly established in 1928 by Dandy's[389] report of nine cases of Ménière's disease successfully treated by section of the eighth nerve. The use of this method in a number of cases was soon reported by Coleman and Lyerly,[390] and by Cairns and Brain.[391] In his first paper, Dandy suggested the possibility of division of only the vestibular portion of the nerve, and this was first done in 1931 by McKenzie,[392, 393] shortly followed by Dandy.[394, 395] The latter[396] actually performed this differential section bilaterally in one case.

Peripheral and Visceral Pain.—The unbearable pain of inoperable pelvic carcinoma, amputation stump "neuroma," and similar painful conditions of irremediable cause has long been amenable to neurosurgical relief. Since its first use by Spiller and Martin,[397] and Frazier[398] at Spiller's suggestion, the operation of anterolateral chordotomy has been of proved value and has largely supplanted the older procedure of

*In 1902, Parry[385] divided the eighth nerve, apparently for Ménière's disease. A similar attempt by Wallace and Marriage[386] in 1904 was unsuccessful. Frazier performed the operation successfully in 1908 for aural vertigo[387] and in 1913 for tinnitus.[388]

posterior root section in this type of case. The results of chordotomy have been recently improved by the researches of Foerster,[399] and Foerster and Gagle.[400] Other recent papers by Schüller[401] and Kahn[402] have reviewed the progress and results of the operation.

Another procedure for the relief of peripheral and visceral pain was introduced by Dogliotti.[403] This consists of the intraspinal injection of minute amounts of alcohol. The method has been extensively employed in this country by Stern,[404, 405] and recent papers by Abbott,[406] Russell,[407] and Adson[408] indicate that it is of definite value in selected cases and in careful hands. Unless it is performed with the greatest care, there is a great risk of permanent motor damage (cf. Tureen and Gitt[409]).

The treatment of other painful conditions will be discussed in the section on sympathetic surgery.

IX. EPILEPSY

A consideration of true idiopathic epilepsy is not within the province of this paper. Able discussions of the subject have been published in recent years by Foerster,[410] Lennox and Cobb,[411, 412] and Fay,[413] among others. With the progress of time, however, various types of convulsive seizures have been removed from the "idiopathic" group and shown to be amenable to specific therapeutic measures.

Since the time of Hughlings Jackson,[414] the focal motor attacks which bear his name have been recognized as due, in many cases, to tumor, scar, or other localized and often removable lesion.

Adequate surgical therapy of traumatic epilepsy has been given renewed impetus by the work of Del Rio Hortega and Penfield,[415] Foerster and Penfield,[416, 417] Penfield,[418] and Wortis and McCulloch.[419] These investigators have thrown great light upon the structural and functional basis of the epileptic seizures and have emphasized the localizing importance of the nature of the attacks and of encephalography, and the therapeutic importance of radical extirpation of cortical scars. The recent literature on traumatic epilepsy has been reviewed by Spurling.[420]

Of great importance is an outgrowth of this work, dealing with focal epilepsy not due to demonstrable gross cerebral lesion. In a careful study of seventy-five cases of Jacksonian epilepsy, Penfield and Gage[421] have pointed out the localizing value of many types of aura and primary convulsive symptoms, even in cases in which the convulsions immediately become generalized. Furthermore, Penfield[418, 422] has withdrawn many of these cases from the "idiopathic" group by proving their focal nature and has shown that the convulsions may be cured by appropriate cortical resection. The exact area involved is located at operation by careful electrical exploration of the cortex. Similarly, Sachs[213] has performed cortical resection for Jacksonian epilepsy without gross lesion in eight

cases. It seems probable that more and more cases, hitherto considered idiopathic epilepsy, will be found to have a focal "trigger-zone," the removal of which will result in abolition of the convulsions.

The description of the syndrome of hyperinsulinism by Harris[423-425] has shown that another large group of convulsive states is due to or exacerbated by hypoglycemia and is amenable to appropriate surgical or dietary therapy. (Cf. also Weil,[426] Carr, et al.,[427] Graham and Womack,[428] Neilson and Eggleston,[429] McGavern[430].)

The study of all forms of epilepsy has recently been spurred by the organization of the International League Against Epilepsy, the American branch of which was organized in 1936 under the presidency of Dr. W. G. Lennox.

X. THE SURGERY OF THE SYMPATHETIC NERVOUS SYSTEM

Modern sympathetic surgery had its beginning with the ramisection for spasticity performed in 1924 by Royle,[209, 210] based on the experiments of Hunter.[431] True, the first cervicothoracic ganglionectomy was done in 1896 by Jonnesco[432] and the first periarterial sympathectomy by Jaboulay[433] in 1899. The latter operation was extensively employed by Leriche,[434-437] but met with little popularity, probably due to the demonstration by Kramer and Todd[438] that the arterial nerve supply is distributed by main nerve trunks rather than along arterial trunks (cf. also Kuntz,[439] and Ranson[440]).

Although Hunter's opinion is not now generally accepted (Ranson[440]), and Royle's operation has not proved effectual for the relief of spasticity, it, nevertheless, resulted in the mushroom-like growth of an enormous new field of surgery. The following year, the use of lumbar ganglionectomy for Raynaud's disease was reported by Diez,[441] and by Adson and Brown,[442] independently; Royle [443, 444] promptly began to employ cervicothoracic trunk section (using an anterior approach) for Raynaud's disease of the upper extremities. A posterior approach with resection of the stellate and second thoracic ganglia was developed by Adson and Brown[445] in 1929.*

The use of sympathetic resection for Raynaud's disease proved very satisfactory from the beginning (Adson,[447] Adson and Brown,[448] Spurling, Jelsma, and Rogers,[449] Horton and Craig,[450] Young[451]), and almost immediately its use began to be advocated for a great many other conditions. As is the case in any new field, many of the attempts have proved fruitless, and others are as yet of uncertain value. In several types of disorder, however, in addition to Raynaud's disease, sympathetic surgery is of great value.

In 1927, Wade and Royle[452] reported a case of Hirschsprung's disease treated by left lumbar ramisectomy. Judd and Adson[453] employed

*Adson and Brown credit Henry[446] with using a similar operation for angina pectoris in 1924.

ganglionectomy the following year, and Rankin and Learmonth[454] sectioned only the postganglionic fibers to the colon and rectum. It is now believed that the more radical procedure (Adson[455]) is necessary, and the results of this operation are strikingly successful.

Resection of the presacral nerve by Learmonth and Braasch,[456, 457] and Adson[458] for cord bladder and other paralytic vesical conditions has resulted in marked improvement, and the same operation gives great relief in selected cases of severe dysmenorrhea (Leriche,[459]* Cotte and Dechaume,[460] Adson and Masson,[461] Shaul,[462] Cannady and Bailey[463]). When employed for chronic interstitial cystitis, however, the results have by no means been uniformly good (Douglass,[464] Van Dusen[465]). Adson, Craig, and Brown[466] have reported the use of cervicothoracic sympathectomy for excessive sweating of the hands (hyperhidrosis) with excellent results, and relief was obtained in similar cases by Roberts,[467] and Leriche and Frieh.[468]

Controversies still continue regarding the surgical treatment of polyarthritis, angina pectoris, and essential hypertension.

Any improvement which follows sympathetic surgery for polyarthritis (first reported by Rowntree and Adson[469]) can result only from an increase in the circulation of the affected joints, and only patients in whom the pain is relieved by local or bodily increase in temperature should be so treated. With careful selection of cases, favorable results may be expected in some instances (Rowntree, Adson, and Hench,[470] Hench and Craig,[471] Spurling and Jelsma,[472] Young,[473] Flothow[474]).

Angina pectoris has been treated by various operations upon the sympathetic nerves since the first operation for this purpose by Jonnesco[475] in 1906. Relief of pain has been often reported, but, at best, the results are variable, the mortality rate high, and the contraindications numerous (cf. Leriche and Fontaine,[476-478] Cutler,[479, 480] Coffee, Brown, and Humber,[481-483] Adson,[455] Danielopolu,[484] MacKenzie,[485] Hofer[486]). In 1925, Mandl[487] reported temporary relief of angina pectoris by the paravertebral injection of procaine, and the following year alcohol was used for the same purpose by Swetlow.[488] This procedure has since been used extensively by White[489, 490] with success in most cases. Empirically, paravertebral alcohol injection gives better results than any but the most radical operations, while being almost entirely free of the dangers of extensive surgical procedures. Scientifically, it has been given a sound rational basis by the recent experiments of White, Garrey, and Atkins,[491] who have shown that all cardiac pain is transmitted over the sympathetic nerves through the upper five thoracic posterior roots. This work also establishes the rationale of the multiple posterior root sections employed by Davis.[492] White and his associates are careful to warn, however, that even paravertebral alcohol block should be used only in selected patients in whom the pain is intolerable and unresponsive to medical treatment.

*Leriche employed only periarterial sympathectomy of the great pelvic vessels.

If essential hypertension, without primary renal or cardiac disease, be characterized by a widespread arterial constriction mediated through the sympathetic vasoconstrictor nerves, then a vasoconstrictor paralysis of a large cross-section area of the arterial bed should result in an improvement in the elevated blood pressure. The renal and suprarenal nerve supply should also be abolished or diminished, thus producing further improvement. This is the basis of several operations recently proposed for this distressing condition. Adson and Brown, [493, 494] and Page and Heuer[495, 496] sectioned the anterior spinal roots bilaterally from the sixth thoracic to the second lumbar, inclusive. Section of the splanchnic nerves subdiaphragmatically by Craig and Brown,[497] and supradiaphragmatically by Peet[498, 499] has been employed, and Adson[455, 500] has recently added partial suprarenalectomy to Craig's operation. Varying degrees of success have been reported with these operations, but it is yet too early to be certain of their ultimate effects. Allen, Lundy, and Adson[501] have stated that the *immediate* effects may be preoperatively predicted by observing the effects of pentothal anesthesia on the blood pressure. Recent experiments by Prinzmetal and Wilson[502] have thrown some doubt on the primary premise stated above by showing that the vasoconstriction may not be of a central neurogenic nature. Time and further investigation should clarify this question.

Operations on the sympathetic nervous system have been proposed or employed for scleroderma (Brown, O'Leary, and Adson[455, 503]), retinitis pigmentosa (Royle,[504] McDonald and McKenzie[505]), and certain types of headache (Love and Adson[506]). Excellent general discussions of sympathetic surgery have been published by Young,[507] Adson,[455] Leriche and Fontaine,[508] Livingston,[509] and Spurling.[510]

XI. THE TEACHING OF NEUROSURGERY

In a telegram to the Harvey Cushing Society, meeting in Rochester, Minnesota, in 1936, Dr. Cushing said, "... [I] venture again to remind the Society in the words of Leonardo that it is a mediocre pupil who does not excel his master." Though to do so may be deemed almost impossible, it is no less a tribute to Dr. Cushing and his contemporaries and older pupils that neurosurgery has attained its present status as a recognized and essential specialty, skillfully and intelligently practiced in all of the university hospitals and most of the larger cities of this and other countries.

This extraordinary growth must be attributed in large measure to the personal teaching and influence of relatively few great pioneers in the field. Neurosurgical centers have arisen in Boston and Breslau, in Philadelphia and Stockholm, in Montreal, Baltimore, New York, St. Louis, Rochester, Chicago, San Francisco, and elsewhere, to which young men gravitate in ever increasing numbers for special training in this field. The establishment of great institutes of neurology and of closer

relationship between laboratories of physiology and pathology and their respective clinics have contributed greatly to the progress of neurosurgery. A growing academic tendency has appeared, particularly in Boston, Chicago and Montreal, to group neurology and neurosurgery together, with neuropsychiatry as a separate field. Such a logical arrangement affords improved facilities for the teaching of students and prospective neurosurgeons alike.

Concomitant with the invaluable personal teaching has come the publication of numerous important texts and sections in systems of surgery. Among recent publications of this kind may be mentioned those of Sachs,[511] Bailey,[512] Spurling,[513] Dandy,[190] Horrax,[514] Adson,[310] Peet,[515] Mixter,[516] Elsberg, [517] and Stookey.[518]

Neurosurgery climbs on, then, to ever greater heights over "the clustered shoulders" of all those mentioned all too briefly in this limited summary and of many others as well. Much progress has been made, but greater discoveries await us.

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Review of Recent Meetings

REVIEW OF THE TWENTY-SECOND ANNUAL MEETING OF THE RADIOLOGICAL SOCIETY OF NORTH AMERICA, CINCINNATI, OHIO, NOVEMBER 30 TO DECEMBER 4, 1936

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THE annual meeting of the Radiological Society of North America produced a number of papers of interest to surgeons. Only those contributions which were outstanding or particularly interesting will be reviewed here. In the first session **Dr. Oscar Lipschultz**, of Minneapolis, presented a paper on **Late Results in Traumatically Displaced Epiphyses.** He reported the end-results in a large series of cases in which reexamination was made from eighteen months to eight years after an injury with displacement or fracture of an epiphysis. Comparison of the length of the injured bone with the normal side and with normal controls was made, and there were observations as to the presence of deformity or other growth disturbance. It appears that trauma to the epiphysis rarely results in functional deformity or disability. There may be some shortening or, in a few cases, some lengthening of the involved extremity, but this is usually insufficient to produce any disturbance of function. Furthermore, it would appear from his results that the degree of reduction of the displaced epiphysis has relatively little relationship to the end-results.

A very illuminating paper by **Dr. Henry Snure** and **Dr. George D. Maner,** of Los Angeles, was presented on **Roentgen Ray Evidence of Metastatic Malignancy in Bones.** Dr. Snure pointed out that in many instances good roentgenograms fail to reveal evidences of metastatic malignancy in bones in which metastases were later found at autopsy. Experimental work indicated that small erosions of the medullary canal could be demonstrated only with great difficulty and frequently not at all in the roentgenogram. Changes in the cortex of the bone were much more obvious. Metastases to the spine are particularly likely to be overlooked. The negative roentgen diagnosis, therefore, is not always indicative of the absence of metastases.

The Incidence and Classification of Hiatus Hernias was discussed by **Dr. Maurice S. Dwyer,** of Seattle. He brought out the importance of the recognition of these hernias, that they are much more frequent than has generally been considered; he described in some detail the various classifications.

Dr. Ray Carter, of Los Angeles, presented a paper on **Noncarcinomatous Tumors of the Stomach,** in which he demonstrated that sarcomas of various types, neurofibromas, and numerous benign tumors, all could be demonstrated by roentgen examination as occurring in the stomach. These noncarcinomatous tumors are probably more frequent than has previously been supposed and their recognition is of great importance.

Experimental work on **The Rate of Emptying of the Gallbladder in Patients With Gastric and Duodenal Ulcer** was reported by **Dr. Edward A. Boyden,** of Minne-

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apolis. Dr. Boyden presented data to show the effect of pregnancy, carcinoma, gastric ulcer, and duodenal ulcer on the rate of emptying of the gallbladder after a standard meal of egg yolks and cream. The curves, which can be plotted from careful measurements of the emptying gallbladder, indicate clearly that both gastric and duodenal ulcers cause increased rapidity of emptying of the gallbladder, while pregnancy causes a marked delay in emptying. The exact mechanism of this effect of ulcer is not entirely clear, but it is possible that the tendency for a preliminary rush of the meal from the stomach into the duodenum, in cases of ulcer, may account for the increased rapidity of emptying of the gallbladder.

Dr. Edward W. Rowe, of Lincoln, Neb., presented a paper on **Primary Tumors of the Small Intestine,** reporting in great detail the findings in eight cases, and calling attention to the importance of repeated examinations of the small intestine roentgenologically, for the demonstration of these tumors which are very often overlooked.

On December 2, there was presented a series of papers of considerable interest. **Carcinoma of the Bronchus** was presented by **Dr. Lewis H. Clerf,** of Philadelphia, who emphasized the importance of both roentgen and bronchoscopic examinations in patients suspected of carcinoma. He paid particular attention to the importance of wheeze as an early symptom and also called attention to the difficulties in bronchoscopic diagnosis of tumors of the upper lobe or of the peripheral bronchi. He directed attention to the fact that in the early stages of a bronchial carcinoma, obstructive emphysema might conceivably be produced, and that the observation of this in a roentgenogram might present a very important, early sign of carcinoma. Close cooperation between internist, roentgenologist, and bronchoscopist is absolutely necessary to achieve a diagnosis of bronchogenic carcinoma.

Roentgen Methods of Studying the Soft Tissue Structures of the Neck were discussed by **Dr. W. Edward Chamberlain** and **Dr. Albert K. Merchant,** of Philadelphia. They reviewed the work that had previously been done on the demonstration of the tissues of the neck, and showed clearly the importance of roentgen study particularly with relationship to tumors of the larynx. Paralysis of the vocal cords can readily be detected by fluoroscopic examination, while tumors extending into the larynx or into the pharynx, inflammatory processes, foreign bodies, and various other types of morbid anatomy can be quite clearly delineated if the proper technic is used. The paper was discussed by **Dr. Brown** and **Dr. Iglauer,** of the University of Cincinnati, who presented numerous cases to emphasize the importance of the roentgen examination of the neck.

Pulmonary Pneumocele, Certain Considerations in Cystic Disease of the Lung was presented by **Dr. Carlton B. Peirce** and **Dr. Paul R. Dirkse,** of the University of Michigan. Dr. Peirce pointed out that not all cysts of the lung are necessarily congenital and that the designation of a cyst as congenital, because of the absence of a definite preceding history of disease, is not necessarily correct. He demonstrated clearly, by a number of cases, that inflammatory processes of the lungs in early childhood may cause stenosis of the bronchus; an air cyst may thus be produced in the lung and in many instances may remain permanently. In cases of this type, seen later in life, the tendency to diagnose this residual cyst as congenital in origin should be curbed. It is clearly possible to produce a pneumatocele as a result of almost any type of inflammatory process in the lung.

On December 3, a symposium on x-ray therapy was held. **Radiation Treatment of Malignancy of the Lip** was presented by **Dr. Ira I. Kaplan,** of New York. He detailed his observations on a series of 147 cases of carcinoma largely of advanced type. The factors which influence the mode of treatment are: (1) position and

size of lesion, (2) presence of ulceration or infection, (3) presence of gland extension, and (4) age of patient. Biopsy is always suggested. All cases have irradiation to the neck area. Heavy doses of x-rays are used, and this is increased when fixed nodes are present. The radium pack is preferred when it is available. The local lesion may be attacked by surgery, radium, x-ray, or a combination.

A paper on **A Study of Radium Technic in the Treatment of Carcinoma of the Rectum** was presented by **Dr. Harry H. Bowing** and **Dr. Robert E. Fricke,** of Rochester, Minn. Radium therapy of rectal carcinoma shows more divergence in methods of treatment than does the treatment of carcinoma elsewhere in the body. This is necessarily so, because of many factors peculiar to malignancy in this situation. Except when a colostomy has been performed, we are treating a part of the body which cannot be immobilized, but must continue its daily function during treatment. Even if a colostomy has been performed, we are treating a field which is always infected and cannot be rendered aseptic. The general state of health of the individual patient has an important bearing on the selection of methods of treatment; we are dealing with an advanced age group with shorter life expectancy, and a large number have concomitant serious diseases of other organs.

Dr. Hayes E. Martin, of New York, gave a paper on **Peroral X-radiation in the Treatment of Intraoral Cancers.** In many intraoral growths, protracted x-radiation is used as a part of the treatment. If given through the skin of the cheeks and neck, adequate dosage may be followed by some late degenerative changes in the skin, bone, or other deep tissues. At least a portion of these untoward effects may be avoided by the use of peroral portals in conjunction with the usual methods of treatment. The technic was described in detail, the tube being placed within the mouth and x-rays given with a shock-proof tube.

The question **Should the Method of Coutard Be Applied in All Cases of Cancer Treated by Roentgen Rays?** was discussed by **Dr. W. Edward Chamberlain** and **Dr. Barton R. Young,** of Philadelphia. It was emphasized that in certain cases the massive dose method was superior to the fractionated dose and that it might constitute a serious error to apply the Coutard method in certain cases. Individualization of cases is of great importance, and the routine use of the Coutard method is to be decried.

An important and original contribution **Studies on the Effects of Neutron Radiation** was presented by **Dr. Robert Stone,** of San Francisco. Dr. Stone and his associates administered RaNa intravenously and intraduodenally in a case of aleucemic leucemia with enlarged lymph nodes. They made careful measurements of the radioactivity of the blood of the patient himself, and of the various excreta during a period of several days. The decay took place almost completely in sixty to eighty-four hours and the elimination during this period was less than 10 per cent. As much as 53 mc. eq. were given without any untoward effects and, likewise, with practically no therapeutic results. In the discussion, **Dr. Robert Newell,** of San Francisco, called attention to the radical difference in the effects of RaNa as compared to RaCl. A dosage of the latter as small as 1/100 of that given by Dr. Stone produced severe—often disastrous—effects. The difference, no doubt, lies in the character of the decay, RaCl giving off alpha rays, while RaNa gives off beta rays.

A symposium on **Gastroscopy and Roentgenology in the Diagnosis of Diseases of the Stomach** was presented by **Dr. Rudolph Schindler** and **Dr. Frederic Templeton,** of Chicago; **Dr. E. B. Benedict** and **Dr. Richard Schatzki,** of Boston; and **Dr. B. R. Kirklin,** of Rochester, Minn. This was followed by an extensive discussion by authorities in these fields. There was general agreement among the

essayists as follows: gastroscopy should always be preceded by adequate roentgen examination of the stomach; with the flexible gastroscope, the procedure is not particularly dangerous, although accidental perforations may rarely occur; gastroscopy is chiefly valuable in the diagnosis of gastritis, hemorrhagic erosions of the gastric mucosa, very small polyps, very shallow gastric ulcers; it may frequently be of value in the detection of larger gastric ulcers, of carcinoma, and other types of tumors, and in the differentiation of benign from malignant ulcers. Gastroscopy is supplemental to roentgenology in the diagnosis of diseases of the stomach. It should be used particularly in those cases wherein persistent symptoms are found but the roentgen examination is negative, and in those in which the roentgen findings are doubtful. Gastroscopy has sharp limitations, particularly as regards the pyloric portion and the fundus of the stomach. It is far superior to the roentgen examination in the diagnosis of gastritis.

The final session was given over to a number of topics. **Skeletal Anomalies and Industrial Injuries** were discussed by **Dr. W. Warner Watkins**, of Phoenix, Ariz. He demonstrated a large number of anatomic variations and anomalies which are familiar to the experienced roentgenologist, but which are often mistaken for fractures or other injuries by clinicians with little experience. Unfortunately their opinions as to the interpretation of roentgenograms may be fully accepted in the courts, with resultant miscarriages of justice.

A symposium on physics occupied the remainder of the program. In the main, this was highly technical. A paper on **The Biological Action of Neutron Rays** was presented by **Dr. John H. Lawrence**, of Yale University, and **Dr. Paul C. Aebersold** and **Dr. Ernest O. Lawrence**, of the University of California. They detailed experiments on mice comparing the effects of neutron rays and x-rays in the killing of the mice and in the destruction of mouse tumors. It appears that the ratio between the lethal dose and the tumor-killing dose of neutron rays is greater than a similar ratio of x-rays. This suggests the possibility that neutron rays have a greater specificity for tumors than x-rays. The work is as yet insufficiently developed to be conclusive.

Dr. Robert S. Stone and **Dr. Paul C. Aebersold**, of San Francisco, presented a paper on **Clinical Application of Physical Measurements of 200 kv. and 1,000 kv. X-rays.** They used a 200 kv. constant potential and a 1,000 kv. radio-frequency x-ray apparatus. The measurements of ionization on the surface and for depth dose indicated that 1,000 kv. x-rays were superior chiefly in very large fields as applied to unusually thick individuals. In such structures as the neck, for example, where penetration of the 1,000 kv. x-rays is very great, there is a disadvantage which nullifies the greater depth dose; namely, the use of several portals is greatly hampered by the effect on the skin on the side opposite the portal of entry. Considerable experience with both qualities of radiation does not yet indicate any extreme advantages in the higher voltage radiation.

THE FORTY-FIFTH CONGRESS OF THE FRENCH SURGICAL ASSOCIATION, PARIS, OCTOBER 5 TO 10, 1936

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AN INTERESTING symposium was held on grafting ovaries; it was published in full in "La presse médicale," October 10, 1936.

M. Mocquot, of Paris, reported on the findings in animal experiments: In general, the results of homografts are not nearly as good as those following autografts. Although some promising physiologic responses have been achieved in grafting ovaries from another animal of the same species and similar age, they have been definitely less successful than reimplantation of the animal's own ovary after castration. Under these circumstances, evidence of ovulation and internal secretion has been observed over a three-year period. Grafting the ovarian tissue within the uterine cavity has been followed by successful impregnation.

Mocquot confirms Halsted's law, that successful takes are more common in the complete absence of glandular secretion. He has found that massive grafts offer too small an area for adequate vascularization. On the other hand, multiple grafts in tiny fragments do not well resist the defense reactions of the organism. The best method seems to be to implant the ovary sectioned into two pieces (Pettinari). Grafts have been made in a great variety of places: in the parietal peritoneum and in the omentum, or within the tubes or the uterine cavity, in order to obtain the passage of ova; in the anterior chamber of the eye for direct observation; and in the muscles when internal secretion alone is to be obtained Signs of regeneration have been observed at the end of a month with new formed follicles and corpora lutea. At the end of several months, the grafted tissue may appear nearly normal, but its bulk begins to diminish little by little. In guinea pigs some of the grafts have used up their follicular reserve at the end of three to four months, nearly always at the end of two to three years. Durable results are increasingly difficult to obtain as one ascends the phylogenetic scale.

M. Cotte, of Lyon, reported on his personal cases of ovarian grafts in women, and reviewed the results published in France and abroad: No lasting results have been seen in homografts taken from another woman and transplanted into one where castration has been followed by characteristic menopausal symptoms. Sippel, the surgeon who has had the greatest experience with this method, has concluded that ovarian homografts are always absorbed after a short period. Similarly, heterografts (from other species) are always destined to be absorbed, notwithstanding some of the reports published by Voronoff.

Good evidence, however, exists that autografts, made by reimplantation of healthy ovarian tissue at the time of operation, can be successful. Their use has two principal indications:

1. In young women whose tubes are hopelessly diseased and for whom salpingectomy is unavoidable, it is occasionally possible to graft a healthy ovary within the uterine cavity. It is much better to transplant the ovary with its pedicle intact than to attempt a free graft. Cotte reports 200 such procedures, followed by pregnancy in twenty-one instances, but a third of these terminated in miscarriage at the third or fourth month.

2. In cases of advanced pelvic inflammatory disease where a salpingo-oophorectomy must be done, Cotte discusses the value of implanting free grafts of small

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bits of undiseased ovary. He states that in well-selected cases such grafts often prevent the symptoms of premature menopause which follow castration.

When employed with judgment in cases where conservative partial resection of the ovaries or salpingectomy is impossible, Cotte concludes that such grafts are worth while. This is particularly true when it is possible to preserve the uterus. In his personal statistics of 92 such cases, where portions of ovary were grafted in the omentum, menstruation was reestablished in 65 out of the 74 patients which were followed. This generally takes place at the end of three months, but in severe cases of pelvic inflammation, it may be delayed for seven months. Histologic examinations of the grafts have shown a reduction in the number of primordial follicles and often a cystic degeneration. As a result, the physiologic activity of such grafts cannot be expected to last as long as that of the normal ovary. Luteinization often occurs without rupture. Examinations of the uterine mucosa made by Bourg show perfectly normal evolution, which is the best test of the physiologic activity of the graft.

THE THIRD CONGRESS OF THE INTERNATIONAL SOCIETY OF ORTHOPEDIC SURGERY

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THE Third Congress of the International Society of Orthopedic Surgery met in Bologna and Rome, September 21 to 25, inclusive, with **Professor Ombredanne,** of Paris, as president of the Society. **Professor Putti,** of Bologna, was president of the Congress and as such did much to make a most impressive meeting for those who were privileged to attend.

Bologna is a particularly suitable place for such a meeting, for several reasons. In the first place, it is a city of considerable historic interest, dating back as it does to the preChristian era. In the second place, it is the site of one of the oldest universities in Europe. The beginnings of this university date back to the eleventh century, when student guilds existed. In the twelfth century the e guilds were grouped together to form the university. At first law was the only subject taught, but later other faculties were added. As Professor Putti pointed out, as early as 1426 a lectureship "in dislocations and fractures of bones" was established. Bologna is also the site of the "Institute Rizzoli," which has been in existence for more than a hundred years as a surgical institution, and from which has emanated some orthopedic procedures of the greatest importance. It has been a leader in the development of modern orthopedic surgery. Finally, Bologna was particularly suitable for such a congress because of the presence there of Professor Putti, who is today one of the outstanding, if not the outstanding, orthopedic surgeons in the world. He has been a leader in this rapidly developing specialty and has made several contributions of major importance to its literature. He is not only an excellent surgeon, but a teacher and leader as well, and because of these attributes and his facility with languages, he is certainly the outstanding member of the International Orthopedic Society. He was the originator of the idea of an International Orthopedic Society, and his presence in the leading rôle made the meeting highly successful.

The meeting opened with the inauguration of the Congress, and several officials of the government as well as of the university spoke. Professor Putti's presi-

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dential address reviewed the development of orthopedic surgery and emphasized the conception of its scope, which originated with his predecessor, Alessandro Codivilla. "This conception," he said, "is synthetically expressed in the formula now universally accepted by which 'orthopaedic' is the synonym of surgery of the organs of movement." He further emphasized the importance of orthopedic surgery in the care of increasing numbers of traumatic cases. The significance of this is emphasized by the fact that the Society later accepted Professor Putti's proposal to change its name from "The International Society of Orthopedic Surgery" to "The International Society of Orthopedic Surgery and Traumatology."

The clinical meetings followed the first day's meeting, and they were devoted to discussion of internal derangements of the knee. Several speakers presented different phases of the subject, one of the principal speakers being **Mr. Harry Platt**, of Manchester, who reported on a series of 762 cases of torn semilunar cartilage. The treatment in these cases has come to be fairly well standardized in the British Isles, where a great many such cases are seen. In our own country, treatment has followed along much the same lines. It was interesting to hear from some of the representatives of other countries the type of operative approach employed in these cases; some of them seemed rather radical.

The second clinical day was devoted to a discussion of the subject of **Arthrorises in the Sequelae of Infantile Paralysis.** The term "arthrorisis" is one not often heard in this country but is apparently widely used in Europe; it means "bone block." The posterior bone block of Campbell has been widely accepted in American and in most European countries, but the Europeans have gone farther and produced bone block operations to stabilize the ankle in all of its four directions of movement, and the knee in the anterior as well as posterior movement. It may also be used in the treatment of joints of the upper extremity. It was difficult to evaluate the results of these operative procedures from the papers presented at the meeting. The posterior bone block of Campbell seems to be a procedure of recognized value. The use of bone block to stabilize other movements of those joints is at least being attempted in Europe, and probably more time should be given before a final evaluation of these procedures is made.

The third day in Bologna was given to the presentation of a variety of papers. One of the outstanding papers during this session was presented by **M. Faldini**, of Milan, on immediate subtrochanteric osteotomy in fractures of the neck of the femur. The form of his presentation set an example for international meetings, inasmuch as he illustrated the procedure with a few simple charts and then gave the substance of his talk in a very short discussion, first in Italian, and then in English, French, and German. Finally, he presented about ten elderly women, all of whom had undergone the operation with excellent results. Several other interesting papers were presented on this day, and during the afternoon the entire Congress moved on to Rome where the remainder of the papers were read, and where an inspection was made of the Orthopedic Clinic in Rome.

The social events were beautifully planned and executed, Bologna with her ancient palaces lending herself admirably to such an occasion. The president's dinner on the first evening was held at the Palazza Podesta, a reception by the Municipality of Bologna at the Palazza Communale and a banquet of the Society at the Institute Rizzoli being the principal events.

Everyone came away with a great deal of satisfaction and all those who attended felt that the meeting had been of high quality and had set a standard for others in the future. The next congress of the Society was set for 1939. It is to be held in Berlin, with **Professor Haglund** as president of the Society and **Professor Gocht** as president of the Congress.

Book Reviews

Neurological Surgery. By Loyal Davis. Cloth. Pp. 429, with 174 illustrations. Philadelphia, 1936, Lea & Febiger. $6.

This book should very well serve the purpose for which its preface says it was written, "to give to the practitioner of medicine easily assimilable facts which will aid him in giving his patient accurate and sound advice." This material, including all fields of neurologic surgery, has not been previously collected into a single volume. It is concise, but it includes the fundamental facts about each condition in well-arranged form. The chapter divisions and subdivisions are made in large bold-faced type with good spacing which makes the book much better as a reference work and more easily read if it is used as a textbook.

A valuable feature is the author's account of his experience which follows the general discussion of a lesion. As a rule the total number of cases observed is included, making it possible for the reader to estimate with what background of experience the author's opinions are weighted. Some of the most important references are given. The illustrations are excellent and the photography is good, but the plethysmographs in Chapter XI in the form in which they are given require too much effort on the part of the reader to be of value in a book of this kind.

A few errors in grammar occur in the text. The style for the most part is clear and direct in this excellent book.

Proctology. By Frank C. Yeomans. Second edition. Pp. 661, with 421 illustrations and 4 colored plates. New York, 1936, D. Appleton-Century Company, Inc. $12.

He who undertakes the task of writing a general text must of necessity try to lend the impression of having an equal interest in all aspects of the subject matter. Rarely does he succeed in his endeavor. The field in which the author's richest experience lies beckons with an appeal which he cannot well conceal. For this lack of balance, the reader, however, is frequently well compensated by the more practical wisdom and mature judgments expressed in the sections of the author's special interest. Most texts written by a single author are likely to be beset with this sin. To this weakness, this book is no exception.

The chapters on the anatomy of the anal canal and rectum, diagnostic methods and preparation for operation, hemorrhoids, fissure, fistulas, and electrocoagulation and surgical treatment of rectal malignancies will be found particularly instructive. In the discussion of amebic dysentery, the author points out that isolation of the organisms is much more likely when swabs are made directly from the ulcers. This method would appear to have considerably more merit than the usual examination of the stool.

Many of the chapters contain historical matter of great interest and carefully selected bibliographic references. Pertinent tables and good illustrations help to clarify the text.

Surgeons who have had experience with operations for imperforation of the anal canal and rectum would not agree with the author's statement that if the rectal pouch cannot be found after a ten-minute perineal dissection, colostomy should be done. The author also is apparently unaware of the important paper of Wood Jones upon the delimitations of the rectum. The author's justification for counting nine out of ten operations for imperforation of the rectum successful when seven died within sixteen days of the time of operation would appear to require explanation. Whereas thirteen figures are employed to depict the variety of anatomic types of imperforation and their variants which may be encountered, the value of a roentgenogram in the inverted posture receives but mere mention, and this important

agency in deciding the order of magnitude of the operation necessary is not illustrated.

In the chapter on prolapse of the rectum, no mention is made in treatment of the Ekehorn posterior rectal fixation, of the strangulation of the prolapsed bowel over a tube by ligatures or rubber bands, and of the Delorme and Whitehead procedures. Most surgeons would find the treatment of this subject matter incomplete without a discussion of these procedures.

In the chapter relating to intestinal obstructions arising in the rectum and pelvic colon, the author states that the time element precludes the employment of roentgenographic aids, thereby indicating how little experience he has had with the problem of acute obstruction of the pelvic colon. He also fails to point out the danger of perforation in obstruction of the pelvic colon. The matter of the management of such obstructions is given no adequate discussion here. The consideration of the management of carcinoma of the rectum is excellent. The author finds radium a helpful adjunct in the treatment of rectal malignancy.

This monograph, however, is a valuable and practical treatise which can be read with profit by anyone who deals with rectal diseases.

Minor Surgery. Edited by Frederick Christopher. Third edition. Cloth. Pp. 1030, with 709 illustrations. Philadelphia, W. B. Saunders Company. $10.

That three editions of Christopher's *Minor Surgery* have been presented in seven years bespeaks a deserved popularity of this book. This text well supplements the crowded curriculum in the teaching of surgery in our medical schools, where as a general rule most of the time is spent on subjects of major importance.

In this third edition, the same excellent plan of the book is maintained, covering general topics in the first seven chapters and presenting a regional minor surgery in the remainder of the book.

That all minor surgery may be of major importance has been recognized, and the details of treatment are sufficiently comprehensive to help avoid many difficulties which often arise in the management of the apparently minor case.

In revision of the text, most of the verbatim references have been reduced to smaller print, making them more distinctive, as well as permitting the addition of a large amount of new material while adding but 132 pages to the book. Many new illustrations have been included to supplement the very excellent group in the previous editions.

In every chapter numerous additions of the results of recent studies have brought the entire subject matter up to date, giving us many new and useful methods of treatment in minor surgery.

The latest work on the process of wound healing is fully discussed. The ambulatory treatment of hernia by the injection method is well covered, although perhaps too briefly. A discussion of the Elliott treatment for chronic pelvic inflammations has been added. The Wangensteen suction apparatus, as an adjunct to postoperative care, is illustrated and discussed. These are but a few of the valuable additions to the book.

A study of the chapter on "The Surgical Interne" will well repay a new resident on a surgical service. He will find there details of daily usefulness.

A few minor criticisms present themselves: The treatment of warts by bismuth injections has not been as uniformly successful as indicated in the new references. The treatment of *Trichomonas vaginalis* infections merits more than the passing reference given it. No mention is made of the newer intravenous anesthetics especially useful in minor surgery. A discussion of suture materials might well be added.

This carefully revised third edition of this book will prove of great value to the general practitioner, consulting surgeon, and surgical house officers.